# THE CLINICAL DIAGNOSIS OF INTERNAL DISEASES

## MUSCLES, BONES, AND JOINTS, NERVOUS SYSTEM, METABOLISM, ENDOCRINOPATHIES

***

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# Part XI

# Diagnosis of Diseases of the Muscles, Bones and Joints

(*Pathological Myology, Osteology and Syndesmology*)

## Section I

## METHODS OF EXAMINATION

Formerly, the diagnosis of diseases of the muscles, bones and joints was looked upon as belonging largely in the domain of surgery, but, today, the internist realizes more and more the relationship of diseases of these parts to general medicine, and sees that he must be able to recognize the various pathological conditions met with in these structures. In this book, however, only the features of distinctly medical interest can be dealt with. For the more definitely surgical features and for the details of differential surgical diagnosis, text-books of surgery should be consulted.

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# A. Examination of the Muscles

On account of the close relation of the muscles to the functions of the motor nerves, the *examination of motility* (active and passive) will be taken up in connection with the examination of the nervous system (see Part XII). As a matter of fact, diseases of the muscles are only rarely *primary.* In the majority of cases, they are *secondary* to affections of the bones, of the joints, of the nervous system, or of other parts.

## 1. Anamnesis

In recording the *anamnesis,* especial attention should be paid to the earlier occurrence of conditions that could lead to *secondary involvement* of the muscles, such as acute infectious diseases (*e. g.,* typhoid fever and acute rheumatic fever), syphilis, trichiniasis or neoplasm.

The *mode of onset* of the muscular trouble should be inquired into; we should ask whether it began suddenly or gradually, and whether with, or without, fever and pain. If *pain* was present, its character should be noted, and we should ask whether it was continuous or intermittent, and whether it occurred only on movement, or also when at rest.

If there has been any *trauma,* direct or indirect, it should be carefully described, and we should ask whether the pains or the disability appeared immediately after the injury, or only sometime later.

In the *parasitic* affections, a history of eating raw pork or sausage may give the clue to *trichiniasis;* if we suspect *echinococcus,* we should

inquire into the possibility of infection from dogs, and in case an *abscess* of the muscles is found, the possibility of infection with *Bacillus mallei* from a horse suffering from *glanders* should be kept in mind, since in human beings glanders often gives rise to abscesses of the muscles.

In cases of "stiff neck" or "lumbago," we should ascertain whether or not *similar attacks* have occurred before, and, if so, to what cause they were attributed.

## 2. Inspection of the Muscles

In the first place, we examine the **general musculature** of the patient. In some, the muscles have always been of small volume; in others, the muscles are voluminous. The *volume* depends partly upon heredity, but largely upon the exercise the muscles have. The relationship of the volume of the muscles to the size of the bones should also be noted.

When a **local trouble** is complained of, the *skin* over the muscle should be carefully examined for evidences of acute inflammation (redness, edema, heat), or of hemorrhage from trauma ("black and blue spots").

Complete *absence* of a muscle, due to congenital defect, will sometimes be seen. Thus the M. pectoralis major, the M. deltoideus, or the M. latissimus dorsi may be absent on one side, the absence being easily recognizable from the change in contour of the part.

Increase or decrease in *volume,* or shortening or lengthening of an individual muscle may easily escape notice, unless a careful examination be made, with *comparison* of the symmetrical regions of the body.

In the upper extremities, it is to be remembered that the muscles of the right arm are usually a little more voluminous than those of the left, owing to greater exercise on the right side. In comparing the volume of the muscles of the two sides, we should examine both the resting muscles and the muscles during contraction.

In *weakness,* or in *paralyses,* of the muscles, typical disturbances of active motility, of attitude, of gait, etc., develop (see Nervous System).

Slight atrophy will occur whenever muscles are not used, though, for the recognition of this *atrophy from disuse,* exact measurements may be required.

## 3. Muscle Measurements

In making *comparative measurements* of the two sides of the body, the tape should be applied at exactly the same level; thus, in measuring the volume of the thigh, it is well first to draw transverse lines at distances 10 cm. apart above the upper margin of each patella, and then to measure the circumference at each of these levels. It is well, also, to make several measurements at each level and to

record the arithmetic mean. A difference less than 0.5 cm. easily lies within the limits of error and should be disregarded.

It goes without saying that the limbs should be in precisely the same position and in the same conditions of contraction or relaxation on the two sides when the comparative measurements are made.

**Enlargement** of the muscles of a part as a whole may be due either to true *hypertrophy,* or to so-called *pseudo-hypertrophy* (due to fatty infiltration). Local enlargements may be due to *muscle-hernias* or ruptures, or to something foreign to the muscle itself (*echinococcus cyst, tumor*).

**Shortening** of a muscle is recognizable by a pathological position of the limb to which it is attached; thus a shortened M. biceps brachii causes flexion of the forearm, and a shortened M. iliopsoas flexes the hip.

## 4. Palpation of the Muscles

Many muscles lie so near the surface that they can be easily grasped by the palpating hand; others lie deep and are more or less inaccessible.

On palpation, we observe the *form* of the muscle, its *state of contraction,* its *consistence,* and its *tenderness on pressure.*

A relaxed muscle normally feels soft, a contracted muscle firm, though the consistence varies with the person and the amount of exercise he takes. Should a relaxed muscle on palpation contain firm strands, fibrosis is probably the cause. Should a mass of bony hardness be felt within the muscle, and it be not in the position of a rider's bone (thigh adductors), it may be the result of a contusion that has caused an injury of the periosteum and dislocation of periosteal tissue into the muscle, with formation of a traumatic muscle osteoma, or it may be part of a myositis ossificans.

Normally, the consistence of a muscle is even throughout. If firmer foci be felt, they are pathological and are due to scars, gummata, tumors, or other cause. Partial contracture of a muscle may be responsible for local increase of consistence in the abdominal muscles when the peritoneum beneath is irritated.

Free fluid, or pus, within a muscle gives rise to *fluctuation* on palpation. It should be remembered, however, that if the testing fingers are applied in a line at right angles to the long axis of the muscle, fluctuation can often be felt in normal muscular tissue; to make sure that a pathological fluctuation exists, we should avoid applying the fingers in the direction mentioned.

After palpating the relaxed muscle, the same muscle should also be carefully palpated in the contracted state; ruptures of the muscle substance, or of the fascia, and resulting *muscular hernias* can often thus be made out.

It is often important, for instance in cancer of the breast, to determine whether or not a pathological process actually involves a muscle, or its overlying fascia. To determine this, one ascertains whether the mass becomes fixed on contraction of the muscle.

On testing the *tenderness* of a muscle to pressure, portions of the muscle should be pressed between two fingers rather than pressed by one finger upon underlying bone, since by the latter method the tenderness elicited may be due to an inflamed periosteum, and not to a tender muscle.

In some processes, the muscle is diffusely tender; in other, the tenderness is local.

## 5. Röntgenology of Muscle

When the consistence of a muscle is altered, and especially if calcification be suspected (as in myositis ossificans, or in muscle osteoma following periosteal displacement from trauma), x-ray examinations are very useful in determining the exact size, form, and position of the calcified mass.

## 6. Histological Examination of Muscle Particles

In some cases, it is desirable to examine bits of muscle microscopically. The muscle for this purpose was formerly obtained by *harpooning,* or by *exploratory puncture* with a needle of large caliber; since, however, local anesthesia can now be so easily obtained, it is customary to *excise* a small bit of muscle with the knife. I have several times arrived at a positive diagnosis in trichiniasis, and, occasionally, in myasthenia gravis, by histological examination of such excised muscular particles. In tumor, in lues, in tuberculosis and in glanders, such histological examination may also be helpful for diagnosis.

## 7. Functional Testing of the Muscles

We test both the *active movements* and the *passive motility.* The active movements may be tested with or without resistance. For testing the strength of the grip of the hand, the dynamometer may be used.

Such examinations give us information regarding *paralysis, paresis* and *contracture.* We observe also any hyperkinetic phenonema (tremor, twitching, spasm, etc.). For an exact analysis of the muscle functions in all parts of the body see Part XII.

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# B. Examination of the Bones

## 1. Anamnesis

In taking the anamnesis, we inquire especially regarding *trauma,* so important as a forerunner of osteomyelitis, of tuberculosis, and even of tumors of bone.

In the diagnosis of *fracture,* a history of the exact character of the injury is very important, since the fractures that follow specific injuries are often extremely characteristic. A man who falls perpendicularly from a tree is likely to fracture his spine. When, on falling, he protects himself by his outstretched hands, he is likely to fracture the radius. When he injures his forearm in cranking the gasoline engine of an automobile or of a motor boat, he is likely to incur a Colles' fracture.

Some persons are particularly prone to fractures, even when the trauma is slight. Such patients suffer from **abnormal fragility** of the bones; this may be *general,* as in osteopsathyrosis, or *local* (tumor, gumma, osteomyelitis, tuberculosis, etc.). When fracture occurs without a history of trauma it is called a **spontaneous fracture.** This is not uncommon in *tabes,* in *tumor,* and in *osteopsathyrosis.* In the latter condition, a history of numerous fractures earlier in life is common.

If the patient complain of **pain in the bones,** its character (boring, pulsating, tearing, dull, aching, etc.) should be inquired into. We should ask whether it occurs only on movement, or also when the parts are at rest, and, especially, whether the pains are worse at night after retiring, since *dolores nocturni,* or so-called *dolores osteocopi,* are very characteristic of syphilitic periostitis. The pain in gout is prone to come on in bed during the early morning hours. The pains when boring in character are called *dolores terebrantes.*

The *age* of the patient may give a clue as to the nature of a bone disease; thus, acute osteomyelitis is common in children, but is rare in adults. Separation of the epiphyses occurs only in children. On the other hand, the bones grow more fragile as age advances, and, as everyone knows, an old person may fracture the neck of the femur by catching his toe in the bedclothes, or by other very slight injury.

The *occupation* of the patient may also be important; thus, phosphorus necrosis of the jaw was formerly common in match factories, and still occurs, sometimes, in industries in which phosphorus is used. Porters often develop kyphosis of the spine.

## 2. Inspection of the Bones

When the shafts of the long bones are soft and become curved, **typical deformities** arise (*e. g.,* bow-legs). If the bones be bent near the

joints, as in genu valgum, the deformity may be less noticeable. Deformities of the feet (talipes), of the hands, and of the spine make up a large part of the studies of orthopedists.

In the spine, we distinguish between angular deformity (*gibbus*), so characteristic of caries of the spine and of some fractures, and curvatures of the spine with convexity backward (*kyphosis*), forward (*lordosis*), or to the side (*scoliosis*).

In the long bones of the extremities, curvature due to softening of the whole bone is most often due to rickets or to osteomalacia, while angular deformities are due to local affections of the bone (*e. g.,* fracture).

Recently, the *length of the skeleton* as a whole (gigantism, dwarfism), and the *length of the extremities,* depending partly upon the stimulus to bone growth, partly upon the time of epiphyseal closure, have interested internists on account of the proven relationships of the functions of certain of the endocrine glands (hypophysis, gonads, thyroid, etc.) to these processes. (See Part XIV.)

Asymmetrical *shortenings* may be due to nervous lesions, or to injuries to the epiphyseal cartilage during growth. Shortening of one leg causes tilting of the pelvis, scoliosis and limping. A shortening of the radius, or a lengthening of the ulna, will cause radial flexion of the hand.

When an extremity, say the lower extremity, is shortened, it is necessary to determine where the shortening has occurred, whether in the foot, in the leg, in the thigh, in the pelvis, or in the joints. Such a determination depends not only upon the general examination, but also upon exact measurements.

## 3. Measurements of the Bones

In making measurements, especially of the extremities, the localization of the so-called **anatomical landmarks** is essential. In the *upper extremity,* the tip of the acromion, the epicondyles of the humerus, the olecranon, the head of the radius and the styloid processes of the radius and the ulna, are the important points. In the *lower extremity,* the anterior superior iliac spine, the tip of the trochanter major, the tuber ischii, and the tip of the malleolus lateralis, are the most important landmarks, though we make use also of the epicondyles of the femur and the head of the fibula.

About the **elbow,** the tip of the olecranon and the two epicondyles are very helpful in diagnosis. When the forearm is flexed at a right angle, these three points, if united by lines, form an equilateral triangle lying in a plane with the humerus, while when the forearm is extended, these three points are at the same level; that is to say, they lie in a plane perpendicular to the axis of the humerus. In order to detect a slight change in these relations, it is well to examine simultaneously the injured arm with one hand, and the healthy elbow with the other.

In measuring the **length of the lower extremity** the two extremities should be placed in exactly the same position. First, the distance between the anterior superior iliac spine and the tip of the lateral malleolus should be measured, and second, the distance from the tip of the trochanter to the same malleolus. If there be a shortening of either distance on one side, or of both, a dislocation or a fracture has probably occurred. If the distance between the iliac spine and the malleolus alone is shortened, we speak of *supratrochanteric shortening;* it is due either to a dislocation or to a fracture of the neck of the femur. If both this distance and the distance from the trochanter to the malleolus be shortened, we speak of *infratrochanteric shortening;* it is due to a fracture below the trochanter.

It is very important, as a control, to determine the **position of the trochanter** as regards the pelvis. For this purpose we have three methods:

(1) The determination of the relation of the trochanter to the *Roser-Nélaton line,* which unites the tuber ischii with the anterior superior iliac spine; normally, the tip of the trochanter lies in this line. Should it project more than $\frac{1}{2}$–1 cm. above it, the trochanter is abnormally high;

(2) The use of *Bryant's triangle,* constructed as follows: The patient lies flat on his back. With a blue pencil, a line is drawn continuing the femur axis above the trochanter; then a perpendicular line is dropped to this line from the anterior superior iliac spine; finally, the anterior superior iliac spine is connected with the tip of the trochanter. The rectangular triangle thus obtained normally has equal sides, while if the trochanter be too high, the side corresponding to the lengthened axis of the femur is shorter than the opposite side;

(3) We may use *Schoemaker's method,* in which a line drawn from the tip of the trochanter to the anterior superior iliac spine is prolonged upon the abdominal wall. Normally, this prolongation cuts the median line in front at the level of the navel, or higher, while if the trochanter be abnormally high, it will pass below the navel.

In fractures and dislocations, the angle, direction, etc., of the fragments must be determined (see Surgical Text-books).

In bone examinations, it is convenient to make use of certain simple *instruments* (tape, measuring compasses, cross-rules, plumb-line, etc.).

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## 4. Palpation of the Bones

On palpation, we can determine the diameter of the single bones and we can make out asymmetrical diminution, or increase, in diameter or in circumference.

Local enlargements connected with the skeleton are *immobile,* and this helps to distinguish them from masses near the bone, though an external mass may become adherent to an underlying bone, and thus be rendered immobile (*e. g.,* a carcinoma of the breast may become adherent to a rib).

The *form* and the *consistence of masses* attached to bones, or originating in them, can be felt on palpation. In case of unimpacted fracture, *crepitation* may be palpable. When tumors or cysts originate within the bone and lead to atrophy of the bony substance over them, the latter may be reduced in thickness to a thin, paperlike layer that crackles on pressure (*parchment crackling*).

In subperiosteal hemorrhage, such as that seen in Barlow's disease, or, sometimes, in cephalhematoma, new bone may form at the periphery and on palpation a steep *circular wall* of bone will be palpable, which, on passing toward the center of the mass, suddenly ceases, giving the impression of a bony defect.

On palpation over tumors of bone, especially angiomata, *pulsation* can often be felt. On palpating the skull, pulsation may be due either to a bony tumor, or to pulsation of the brain felt through a bone defect.

In fractures of bones, careful palpation will yield clues to the exact nature of the *deformity* and *displacement.* In diseases of the upper cervical spine, palpation over the pharynx gives access to the vertebral bodies; in diseases of the pelvic bones, palpation through the rectum or through the vagina may be helpful in diagnosis.

In testing the bones for *tenderness on pressure,* we may use (1) gradually increasing pressure, and (2) tapping with the fingers or with the percussion hammer. By such tests on the spinous processes of the vertebrae, disease of the spine may often be easily localized.

Tenderness of the bones may be *diffuse* (as in leukemia, and especially in osteomyelitis), or it may be strictly *localized,* as in fractures, or in bone abscesses.

An important method of eliciting bone tenderness is by *compression in the long axis;* thus, one may press upward from the elbow toward the

shoulder in testing the humerus; from the heel toward the pelvis in testing the lower extremity; or from the head or shoulders toward the pelvis in testing the spine. In making such compression in the long axis, especially in the spine, the greatest care should be exercised, since in disease of the axis, the dens epistrophei may be broken off. In case of impacted fractures, manipulation should be most careful, or the impaction may be undone.

In testing the *consistence of bones* in osteomalacia and in rickets, it may be possible to demonstrate an abnormal softness by passive curvature.

Clues to exaggerated *fragility of the bones* may be yielded by the anamnesis, or by the discovery of numerous calluses or deformities that have resulted from preceding fractures, either intra-uterine or postnatal.

Mobility, where normally there is none, is a sign of *solution of continuity,* and points either to unimpacted fracture or to pseudo-arthrosis. To discover such abnormal mobility in the neighborhood of joints, one should try to produce movements that do not occur normally in the joint. In unimpacted fracture of the neck of the femur, the lower extremity can be shortened by compression in the long axis, or lengthend by traction in this axis. Such abnormal mobility is usually associated with *local pain;* absence of such pain points either to an old lesion, or, if recent, to analgesia due to tabes or to syringo-myelia.

On finding *crepitus* near a joint, we have to make out whether it is in the joint itself or is due to a fracture of bone, or to separation of the epiphysis near the joint. In crepitation due to a fractured rib, the crepitation may be audible during the respiratory movements. Fractures are not always accompanied by crepitation, since the ends of the bones may not be in apposition owing to marked separation or to erosion of the ends of the bones from tumor; or, again, crepitus will be absent if the fracture be incomplete, as in the green-stick fracture of young people, or if the fracture be impacted.

Palpation may be extended and refined by the use of a *probe* in case a fistula or a sinus exists. If the bone be bare, on probing, the raw bone can be felt as grating; if it be insensitive, the bone is necrotic. Sometimes a necrotic bone can be moved slightly with the probe (loose *sequestrum*).

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## 5. Röntgenology of Bones

A large part of the difficulty formerly obtaining in the diagnosis of bone lesions has been removed by the introduction of x-ray methods. In no other part of the body has röntgenology proved more helpful than in pathological osteology. In röntgenograms, we cannot only see the surface and the outlines of the bones, but we can also recognize dislocations and enlargements (and their extent), and, in addition, we can get a very clear idea of the condition of the architecture within the bones themselves and draw deductions therefrom regarding the histological and the chemical state of the bones (osteosclerosis, osteoporosis, halisteresis).

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## 6. Examination of the Skeletal Functions

When the bones are softened, or when there has been solution of continuity from fracture, the function of a bone as a supporting organ can no longer be fulfilled. On attempting to use the bone as support, so much pain is caused that the attempt is given up. When pain is not felt, we have to think of syringomyelia or of tabes.

### 7. Influence of Bone Lesions on Neighboring Parts

In fractures of bones, there is accompanying *hemorrhage.* The blood sooner or later reaches the surface, causing black and blue spots beneath the skin. In fracture of the skull, there may be *bleeding from the ear or nose,* or there may be *extravasation into the orbit,* causing, successively, exophthalmos, subconjunctival hemorrhage, and hemorrhage beneath the skin of the eyelids.

In suppurative osteomyelitis, the inflammation may extend to the tissues about the bones and cause *edema* of the overlying skin.

In tuberculosis of the bones, *cold abscesses* often form, and the pus may wander to long distances from the original source. Thus, an abscess pointing in the groin may be the first recognizable symptom of caries of the thoracic spine; or caries of the lumbar spine may first manifest itself in an inability to extend the hip, owing to psoas abscess; caries of the cervical spine may give rise to cold abscess palpable with the finger in the posterior wall of the pharynx.

Diseases of the bones of the skull and of the spine often lead to *nerve injury,* to secondary injury of the brain, of the spinal cord, and of the roots of the cerebrospinal nerves (see Part XII). Or *visceral injury* may occur. Thus, diseases of the bones of the thorax may involve the heart, lungs, pleura, or mediastinum, while diseases of the pelvic bones often lead to compression of the urethra or to disturbances of the bladder and rectum.

The *state of the body as a whole* will often throw light upon the nature of a bone disease. This is especially true in syphilis, in tuberculosis, and in carcinoma. It should be remembered that carcinoma of the thyroid and carcinoma of the prostate are particularly prone to metastasize in bone.

## C. Examination of the Joints

### 1. Anamnestic Data

In the anamnesis, data regarding the *family history* (gout, hemophilia), a history of *trauma,* or of a general or local *infection,* mode of *onset, pain,* the number and sequence of the *joints involved, nocturnal exacerbation, tenderness, swelling, limitation of motion,* and *creaking* or *grating* may be obtained. The *age* is important. Thus, Still's disease occurs in childhood; acute and chronic infectious arthritis is common in youth and in middle life; hypertrophic osteo-arthritis is a disease of advanced life; and gout usually appears in early middle life.

A *history of hemophilia* will give the clue to bleeder's joint. A history of attacks of *sudden fixation* of the knee-joint will make one think of

a "joint-mouse." The *severity of the pain* may aid diagnosis, for the pain is usually very severe in gout and in gonococcal arthritis. In a child, pain in the knee may be due to disease of the hip. Certain maladies tend to attack special joints; thus the *site of predilection* in gout is the *metatarsophalangeal* joint of the great toe, while the knee is the joint most likely to be the site of a *dérangement interne.*

## 2. Inspection and Palpation of Diseased Joints

Here we consider the following points:

(1) Whether there is any **enlargement** of the joint, and if so whether this is due (a) to *bony enlargement,* (b) to *thickening of the soft parts,* including the skin, the subcutaneous tissue and the joint capsule (bogginess), or (c) to accumulation of *fluid* within the joint (*fluctuation*).

If there be **fluid** in the *knee-joint,* the patella "floats"; one surrounds the joint with his hands so as to prevent the escape of fluid in any direction, and then makes sudden, quick pressure on the patella with his finger. If an abnormal amount of fluid be present, the patella will be felt to hit against the bone beneath and to rebound when the pressure of the fingers is removed.

In the *elbow-joint,* fluid accumulates on both sides of the olecranon; in the *ankle-joint,* in front of and behind the malleoli.

Marked thickening of the capsule (*fungous arthritis*) is commonest in tuberculosis; bony enlargement is commonest in hypertrophic osteo-arthritis; fusiform swellings and true ankyloses in chronic infectious arthritis.

(2) Whether there is any **distortion** of the joint, or **irregularity in contour.** This may be due (a) to *marginal lipping,* (b) to *osteophyte production,* as in hypertrophic osteo-arthritis, (c) to a *ringlike constriction* at the line of the joint, as in the end-stages of infectious forms of arthritis and in the so-called atrophic arthritis, (d) to *localized bulgings of the synovial sac,* (e) to *tophaceous deposits* (gout) or, (f) to *lipoma arborescens,* especially beneath the malleoli.

(3) Whether there is **abolition** or **limitation of motion,** active or passive. This may depend (a) upon true ankylosis (*ankylosis vera*), in which there is a union of the joint surfaces themselves, or (b) upon false ankylosis (*ankylosis spuria*), in which there is no intracapsular union, but only rigidity of the capsule or of the peri-articular soft parts. Limitation of motion, not due either to true or to false ankylosis, may depend (c) upon osteophytes, upon gouty tophi, upon muscle spasm, or, merely, upon pain and effusion. The *angle* within which movements are still possible, or in which the joint is fixed, may be exactly measured by means of a *goniometer;* an approximate idea of the degree of involve-

ment in unilateral affections may be gained by comparing the functions of the diseased with that of the healthy side.

Fixation of a joint due to active contraction of the muscles disappears under deep *narcosis;* it often diminishes much in *sleep.*

In *testing the mobility of a joint passively,* one grasps the parts above and below the joint with either hand and makes passive motions in all the directions in which the joint is normally mobile (flexion, extension, adduction, abduction, rotation). If the affection be unilateral, one compares the mobility of the joints of the affected side with the mobility of the same joints on the normal side.

It is sometimes difficult to distinguish limitation of motion due to *muscle spasm* from that due to osteophyte production or to other organic change in or near the joint. Thus, in the *hip joint,* movement may be limited by (a) pure psoas spasm, or (b) spasm of all the muscles about the joint. In the former case, the thigh is usually a little flexed upon the pelvis, though this flexion is sometimes obscured by lordosis of the lumbar spine. If **psoas spasm** be slight, it is best demonstrated by placing the patient prone on a table and attempting hyperextension. In this test, one stands on the right of the table, places his left hand over the small of the back, and grasping the patient's leg just above the ankle, flexes the knee to a right angle and then lifts the lower extremity so as to overextend the hip. In pure psoas spasm, extension of the hip is the only movement of the joint that is limited.

In *general spasm* of the muscles about the hip-joint, the patient is asked to lie on his back with the lower extremity flexed, both at the knee and at the hip. One then tests abduction, adduction, strong flexion and rotation, and compares the limits of the excursions possible with those obtainable in the sound leg.

When motion is limited by *osteophytes,* or by *marginal lipping,* rather than by muscle spasm, the movement is free until an obstruction is met, when the motion is arrested suddenly, completely and often without much pain. In muscle spasm, the motion is not wholly free even at the beginning, and passive movement becomes increasingly more difficult; it is not suddenly arrested, and one has the feeling that, if he were willing to cause the patient more pain, the excursion of the passive movement could be made greater. When motion is limited by *thickening of the capsule,* or by *adhesions,* the excursions become greater after active exercise or after passive motion; that is to say, after the patient has "limbered up" his joints.

In testing the mobility of the joints of the *spine,* the patient, undressed, stands with knees and hips rigid, and then bends his trunk as far as possible (1) in each of the four main directions (forward, backward, to the right, and to the left), and (2) on rotation, to the right and to the left.

Under the regional examinations of the muscles, bones and joints, many other points in diagnosis and especially in differential diagnosis, will be referred to.

(4) Whether certain **other abnormalities** exist, including (a) *crepitus, grating* or *creaking;* (b) *excessive motion* (such as over-extension, over-flexion or movements in false directions), and *pain* on pressure, or on movement; (c) *free bodies* in the joints (*corpora libera articulorum*); (d) *sinuses* (abscess; tophaceous deposits; bone necrosis; caries); (e) *shortening,* due to telescoping of the joints; (f) *luxations* or *subluxations* often recognizable by loss of the normal directions of the axis of a limb or of a bone; (g) *trophic lesions* of the adjacent skin and muscles (mottling, cyanosis, glossiness, and perspiration of the skin; Dupuytren's contraction; muscular atrophy). Absence of pain despite grotesque changes in the joint structure on palpation and on x-ray examination points to a neuropathic arthropathy (tabes or syringomyelia).

## 3. Examination of Diseased Joints with Rontgen Rays

On x-ray examination, the anatomical condition of the *bones* and *cartilages* of the joints is clearly revealed, and much can be learned also regarding the state of the *soft parts* surrounding the joints, the *synovial membrane* and its *villi,* and the recesses of the *joint cavity,* especially if the joint be previously injected with oxygen gas.

A röntgenogram gives us information immediately as to the presence or absence of (1) periarticular swelling, (2) luxations or subluxations, (3) pathological deviations, (4) narrowing of joint slits, (5) atrophy or destruction of cartilage, (6) erosion of subchondral bone on the articular surface, (7) rarefaction or condensation of bone due to increase or diminution of lime-salts (due to osteoporosis in the one case and to osteosclerosis in the other), (8) distortions of bone evidently due to softening and pressure, (9) gouty tophi, (10) cysts, (11) osteophytes and exostoses, (12) subperiosteal swellings, (13) fibrous or bony ankylosis, (14) calcified free bodies, (15) calcification or ossification of ligaments, and (16) lime-deposits in bursae.

One of the most striking features often to be met with in x-ray plates is the evidence of so-called **acute bone atrophy** (Sudeck, Hale White, Kienböck, Exner). While a certain amount of rarefaction (*osteoporosis*) may result from inactivity or immobility, the very marked examples of "acute bone atrophy" are thought by some to be due to reflex trophic influences; others feel sure that even the marked examples are due to disuse or to local toxic influences.

In the x-ray findings we have to deal entirely with form-relations and the *inferences* that can be derived therefrom. Radiographers help clinicians most when, in their reports, they discriminate sharply between

(1) the objective *morphological findings* in the x-ray plates, and (2) any *interpretative impressions* that they may make regarding probable etiology or probable clinical type. Unfortunately, most physicians press röntgenologists for the latter, and take but little interest in the former.

## 4. Exploratory Puncture and Exploratory Arthrotomy

**Exploratory puncture** will throw light upon (1) the cell contents of an effusion (*cytodiagnosis*), (2) the bacterial contents, through stained smears, cultural methods, or animal inoculations (*bacteriodiagnosis*), and (3) the presence or absence of antibodies to various antigens (*immunodiagnosis*). The puncture should be performed under strict aseptic precautions, preferably by means of a Record syringe and a needle of not too small caliber. The methods of examining such puncture fluids are the same as those recommended for the study of punctates from serous cavities (see Part III).

**Exploratory arthrotomy** may be resorted to for diagnosis in cases where disintegration of a joint is obviously threatened and the nature of the process is obscure. In such instances, incision and perhaps drainage of the joint are indicated for therapeutic reasons, and advantage may be taken of the opportunity to confirm or extend the diagnostic data.

## 5. Diagnosis ex juvantibus; Diagnosis ex nocentibus

Under this heading we may consider the effects of certain therapeutic measures in as far as they bear upon diagnosis.

**Rest** in the recumbent position will usually lead to an improvement of symptoms in cases of *spondylitis,* but not in cases of *tumor of the spine* compressing the spinal cord or the nerve roots.

**Massage,** cautiously applied, may cause improvement in cases of *chronic gonococcal arthritis* and of *chronic traumatic arthritis,* but, in cases of *chronic tuberculous arthritis,* it will exaggerate the symptoms.

**Antiluetic treatment** (Hg; KI; salvarsan) will yield favorable results quickly—almost magically—in the *arthritis of hereditary lues,* and in the *arthritides of the secondary and tertiary stages of acquired lues,* but will be of no avail in *tuberculous arthritis* or in *chronic infectious arthritis* that is non-luetic.

**Salicylates** have an extraordinary effect in controlling the pain of *acute rheumatic fever.* They may also have some pain-stilling effect in other forms of arthropathy, but it is far less striking.

**Colchicum** or **atophan** may exert a magical pain-stilling effect in the arthritis of gout and be unavailing in arthritis due to other cause.

## 6. The General State of the Body in Joint Disease

In studying any arthropathy, the examination should extend to the body as a whole; it should by no means be limited to the joints themselves.

Thus, in joint diseases, the existence of *fever,* of *chills,* of *polymorphonuclear leukocytosis,* and of general *glandular enlargement* with joint involvement, usually points to an arthropathy of the acute infectious type, or to an acute exacerbation of a chronic infectious arthritis.

*Tuberculin tests,* the *gonococcal fixation test,* the *Wassermann reaction,* or the *determination of the coagulation-time,* or *the bleeding-time,* may help in a decision as to etiology.

Examinations of the *nervous system* prevent one from overlooking a tabetic or a syringomyelic arthropathy.

The state of the *tonsils,* of the *endocardium,* and of the *pericardium* may give information regarding true rheumatic fever and other forms of infection.

All possible *primary foci of chronic infection* (*q. v.*) should be closely examined. In males, especially, the examination of the *urethra, prostate* and *seminal vesicles,* with microscopic study of stained smears of the milked-out secretion, may reveal a gonococcal etiology. *Blood-cultures,* and *cultures from enlarged regional lymph glands,* made by Rosenow's method, may permit us to determine the causal agent in the infectious types.

Any accompanying *skin lesions* (erythema multiforme, eczema, psoriasis, purpura, urticaria) should be noted and valued for differential diagnosis.

In families of *bleeders* the occurrence of hemophilic arthropathy must be kept in mind.

Not infrequently the *course of the disease* gives clues as to its nature. Thus, we have already pointed out that the *effects of therapy* (rest, massage, Hg, salvarsan; KI, salicylates, colchicum), may help in the diagnosis. When *gouty tophi* are suspected, the deposit should be needled, and any minute particles secured on the end of the needle rubbed up in a drop of water on a glass slide and examined under the microscope for crystals of mononatrium urate. The shape of these crystals is characteristic and if desired the murexid test may be used in confirmation.

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# D. Regional Examination of the Muscles, Bones and Joints

In studying the body for diseases of the muscles, bones and joints, a knowledge of the conditions that may be met with in the several regions is of special importance. Here, the diagnostic points must be very briefly dealt with. For a fuller account, the treatises of Pearce Gould and of de Quervain may be consulted.

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*See also: English Translation.*

## 1. Examination of the Head

### (*a*) *Fractures of the Skull*

In the head, the examination of the bones of the skull may be very important. In *fracture of the skull* there may be local pain, displacement of fragments, false motion, or hemorrhage. After any injury to the head the physician should always inquire concerning the occurrence of *hemorrhage from the ear, mouth and nose.* In the case of the ear, one should make sure that the blood has not reached the auditory canal from the outside. Copious bleeding from the ear, or bleeding lasting sometime, points to fracture of the base of the skull. Bleeding from the nose or mouth, not due to direct injury to the face, may result from fracture of the ethmoid or sphenoid, or of the pars basilaris of the occipital bone.

### (*b*) *Conditions Causing Exophthalmos, Hemorrhage or Escape of Cerebrospinal Fluid*

If, after a head injury, exophthalmos occur, followed later by conjunctival hemorrhage, and still later by a discoloration of the lids, there has been a *surgical lesion of the orbit,* probably fracture of its roof. Such fracture often occurs by *contre-coup.*

Hemorrhage appearing behind the ear a day or two after a head injury, suggests *fracture of the posterior or middle fossa of the skull.*

Clear fluid from the ear or nose, following head injury, if it contain

but little albumin and much NaCl, is cerebrospinal fluid and points to fracture.

Paralyses in the domain of the cerebral nerves may also follow head injury and be due to fracture of the skull.

Unilateral exopthalmos, accompanied by diplopia, should excite suspicion of *tumor* originating in the base of the skull or in the maxilla (sarcoma). Unilateral exophthalmos developing gradually after trauma, along with pulsation of the eyeball and an audible bruit in the temporal region, points to *rupture of the A. carotis interna into the sinus cavernosus,* due to fracture of the base of the skull. A similar exophthalmos pulsans may be due to *aneurism of the ophthalmic artery* or to *cavernous angioma* of the orbit.

Acute exophthalmos, either unilateral or bilateral, is most often due to a *retrobulbar hemorrhage,* depending upon fracture of the base of the skull, though it may also follow *retrobulbar thrombosis* or *orbital abscess.* The protrusio bulborum of *exophthalmic goiter* may appear suddenly, but usually comes on gradually. It may be unilateral at first but, as a rule, is bilateral from the beginning. It is accompanied by struma, tachycardia and tremor.

### (c) *Inflammations of the Bones of the Skull*

*Acute periostitis* and *osteomyelitis of the bones of the skull* are rare conditions, but they sometimes occur. They should not be considered until other commoner processes (*mastoiditis, erysipelas of the scalp,* etc.) have been ruled out.

### (d) *Tumors and Other Masses in the Head*

When abnormal masses appear in the head, we may have to deal with *cysts* or with a *tumor.* In childhood, *meningocele* and *encephalomeningocele* should be borne in mind. *Dermoid cysts* and *wens* are not uncommon in the head; the former are usually found in the region of the orbit, the latter may be met with anywhere in the scalp or neck.

*Osteoma* of the skull is not uncommon and is recognizable by its ivory consistence. *Neurofibromata* of the scalp are very characteristic and are associated with signs of von Recklinghausen's disease in other parts of the body. I remember very well a patient whom Dr. Harvey Cushing presented at the Johns Hopkins Medical Society, in whom the soft parts on one side of the head, including the ear, had undergone great enlargement and hung down as a pendulous mass beside the neck.

*Gummata* of the scalp are usually multiple. They undergo softening in the center and, if they break down, the base of the ulcer has a yellowish tint and eroded bone can usually be felt with a probe. *Tuberculosis* of

the skull, seen occasionally in children, is associated with tuberculosis of the lymph glands of the neck.

*Primary sarcoma* of the skull occasionally occurs, but *metastatic carcinoma* is more common, often appearing as slowly developing bosses in different parts of the skull. A röntgenogram may reveal many metastases that have caused no palpable enlargement.

### (*e*) *The Maxilla and the Mandible*

In the region of the jaws, fracture is not uncommon. *Fracture of the upper jaw,* or maxilla, may involve the alveolar process (in tooth extraction), or any part of the bone in revolver wounds in attempted suicide. A *fissure-fracture* may occur without wound of the soft parts. Sometimes the only thing complained of by the patient is that his upper teeth have become too long, or he may have persistent, circumscribed pain in the region of the fracture.

A *fracture of the lower jaw* (mandible) is usually easily recognized, though the instances in which the fracture involves the ascending ramus may cause some difficulty. Dental surgeons have done great service in the development of the therapy of fractures of the mandible.

*Dislocation of the mandible* is a common malady, recognizable even by the laity through the displacement forward of the lower jaw and the open mouth, which cannot be closed. Some patients suffer repeatedly from this dislocation, owing to the relaxation of the ligaments of the jaw joints.

**Lockjaw,** or inability to open the mouth, may be due to various causes. In tetanus, the history of previous injury, the risus sardonicus, and the frequently associated unilateral facial paralysis, make the diagnosis clear. Trismus may also be of nervous origin (hemorrhage in the inferior frontal gyrus, pontile tumor).

Other causes of inability to open the jaw include, periostitis of the jaw, actinomycosis, tuberculosis and osteomyelitis. Difficulty in opening the mouth may also accompany arthritis of the jaw joints, severe stomatitis, or severe inflammations in the neighborhood (quinsy).

In differentiating the **inflammatory affections** of the jaws, it is well to bear in mind that *acute periostitis,* when non-luetic, is nearly always due to an infected tooth, and that *primary osteomyelitis* of the jaw is exceedingly rare. Necrosis due to *amebic invasion* has been reported by Flexner. The *chronic inflammations of the jaw* may be secondary to dental infection, or may depend upon infection with actinomyces or upon phosphorus-necrosis.

In **actinomycosis of the jaw,** the firm infiltration, the areas of softening, the involvement of the skin over the jaw, the absence of enlargement of the lymph glands, and especially the presence of sulphur bodies in the pus from the discharging sinuses, are characteristic.

In **tuberculosis of the jaw,** the diagnosis depends upon the insidious onset, the involvement of the ascending ramus of the lower jaw, the ob-

vious tuberculosis of the glands of the neck, and the formation of a cold-abscess beneath the temporal muscle, due to the wandering upward of the pus between the pterygoids and the bone.

In **phosphorus-necrosis,** there is pain in the teeth, which loosen and fall out; abscesses develop with fistulous formation; there is subperiosteal thickening, and finally, necrosis of the jaw with sequestrum formation. The process occurs gradually (in stages), and not all at once, as in acute osteomyelitis of the jaw.

**Tumors of the maxilla** are often mistaken in their early stages for periostitis of the jaw or for maxillary sinusitis. As de Quervain emphasizes, every swelling of the upper jaw, no matter how slight, if accompanied by persistent neuralgic pains, should excite the suspicion of malignancy.

In ruling out *maxillary sinusitis, periostitis* of the jaw and *dental cysts,* x-ray examinations are very helpful. In dental cysts there is a gradual enlargement of the bone, sometimes with parchmentlike crackling. The process is, as a rule, painless and slow of development. One tooth may be missing in the series, and the röntgenogram reveals it in the cyst.

Of the **tumors of the lower jaw,** sarcoma is the most to be feared. It may begin in the periosteum or inside the bone. Any enlargement of the mandible should be viewed with suspicion until one is sure of its benignancy. Benign tumors, as a rule, grow more slowly than malignant growths here, but a sarcoma may be several years in developing. Benign tumors are usually painless, while persistent neuralgia should excite suspicion of malignancy. Sarcomata of the jaw are not associated with enlargement of the regional lymph glands.

Among the *benign growths* occurring in this region may be mentioned fibromata, enchondromata, osteomata, dental cysts and multilocular cystoma of the jaw.

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## 2. Examination of the Neck

In the neck, the attention should be directed especially (1) to the M. sternocleidomastoideus, (2) to the cervical spine, and (3) to the conditions in the several triangles of the neck.

### (*a*) *Abscesses in the Neck*

In the *upper part of the neck,* acute processes are usually dependent upon inflammations of the lower jaw, of the salivary glands, or of the lymph glands. Abscesses in the region of the M. sternocleidomastoideus are nearly always gland abscesses secondary to angina, eczema of the head, or dental infection; a rarer cause of gland abscess here is infection from the esophagus.

An abscess in the *supraclavicular fossa* is usually due to extension from suppuration of the lymph glands higher up, though it may depend upon suppurative osteomyelitis of the clavicle.

Abscess in the *anterior triangle* of the neck usually originates in the thyroid gland, though myositis of the M. sternocleidomastoideus, or osteomyelitis of the manubrium sterni, or phlegmon of the anterior mediastinum, may be responsible.

In the *back of the neck,* abscesses are more common than in front. If situated behind and below the mastoid process, in association with otitis media, an abscess probably depends upon rupture of a suppurative mastoiditis into the neck (*Bezold's abscess*). The back of the neck is also a common site of *carbuncle,* common in diabetes and in cachectic states, due to *Staphylococcus aureus.*

Occasionally, an abscess in the back of the neck depends upon *osteomyelitis of the occipital bone,* or upon suppurative inflammation of a tumor of the neck (dermoid, lipoma).

**Chronic abscesses in the neck** are nearly always *tuberculous* in origin (*cold abscess*), due to tuberculosis of the lymph glands or to tuberculosis of the cervical spine, abscesses of the latter region being situated behind the thyroid and behind the A. carotis. They will rarely be mistaken for other lesions, though a *tumor* originating in the spine or in the deep muscles of the neck may be confused with cold abscess. An *esophageal diverticulum* projecting into the neck might, on superficial examination, be confused with tuberculous abscess.

If a chronic abscess be very firm, or of wooden consistency (*phlegmon ligneux* of Reclus), we should suspect *actinomycosis* and look for foci of softening and for sulphur granules.

When a **cervical fistula** exists, and there is no history of trauma to account for it, we should seek a tuberculous, a syphilitic, an actinomycotic, or a branchial cystic origin.

### (*b*) *Neoplasms and Other Solid Masses in the Neck*

When a firm mass is found in the neck, it may be (1) *inflammatory* in origin, in which event it is probably either tuberculous, gummatous, or actinomycotic; (2) a true *tumor;* (3) an enlargement of the *salivary glands,* of the *thyroid gland,* or of the *lymph glands* of this region; (4) an *aneurism;* (5) an *esophageal diverticulum,* or (6) a *cervical rib.*

In the anterior triangle of the neck, *enlargements of the thyroid* are found (*diffuse struma* of colloid goiter and of Graves's disease; *circumscribed struma* or *struma nodosa;* and *struma maligna*). Masses in the

lateral region of the neck may be due (1) to *enlargement of the lymph glands* (simple lymphadenitis, tuberculosis, syphilis, leukemia, Hodgkin's disease or other pseudoleukemic diseases, lymphosarcoma, metastatic carcinoma); (2) to *cysts* (lymph cysts, branchial cysts); (3) to *aneurism* and *angiomata* and *sarcomata;* (4) to *solid tumors* (lipomata, fibromata, sarcomata, branchiogenous carcinomata, carotid gland tumors).

In the back of the neck, masses may be due to *meningocele, meningoencephalocele, dermoid cysts, sebaceous cysts, lipomata, fibromata,* or *sarcomata.*

Lipomata occur in different forms in the back of the neck. The simplest form is the unilateral encapsulated lipoma. A bilaterally symmetrical lipoma not infrequently occurs here; also the so-called periganglionic lipoma, in which there are accumulations of fat about the lymph glands in this region and elsewhere in the body. To a thick layer of fat that surrounds the neck like a collar, the name Madelung's fat neck has been applied.

### (c) *Stiff Neck and Wry Neck*

An abnormal position of the head and neck may give the clue to diseases of the muscles, bones or joints of this region. A **stiff neck** may or may not be painful. If movements of the neck are *painful,* the joints of the cervical spine become fixed by the surrounding muscles. If the muscular fixation involve the muscles of the two sides equally, the head maintaining a median position, the cause of the pain is also probably medial; while if the fixation involve one side more than the other, and the head be asymmetrically placed, the painful disturbance is also probably unilateral.

When, in stiff neck, the head is held *straight,* the trouble is usually in the *cervical spine.*

If the stiffness has come on suddenly and has followed a severe trauma, it is most often due either to *total dislocation* of a cervical vertebra or to *dislocation complicated by fracture* of the spine. Occasionally, a severe *contusion* or a *distortion,* without fracture or luxation, may be responsible.

If there be no history of trauma, and the stiffness has come on suddenly with fever and chills, we must suspect an *osteomyelitis of the cervical spine.*

If the stiffness of the neck has gradually appeared, and the head is held straight, the commonest cause is *tuberculosis of the cervical spine,* more rarely a developing *neoplasm.*

When the neck is stiff and the head is inclined to one side **(wry neck),** the condition may be due to any one of several causes.

If it has occurred suddenly, it probably depends upon a *myositis* involving the M. sternocleidomastoideus of one side, but it must be remembered that *inflammations of the lymph glands* beneath the sternomastoid muscle, secondary to a sore throat or to an infected tooth, may simulate myositis.

If a trauma have preceded, the acute wry neck may be due either to a unilateral dislocation (*rotation luxation*), or simply to strain (*distortion*).

A *spondylitis* leading to a unilateral injury of the spine is sometimes the cause of painful wry neck.

The cases that most often puzzle the physician, however, are those of *chronic wry neck without pain*—the so-called **muscular wry neck** or **caput obstipum.**

The majority of these cases are due either to an intra-uterine or a postnatal infectious *myositis*. The trouble dates back, usually, to early childhood, and the whole skeleton undergoes changes as a result of the abnormal position of the head. The *skull* itself is asymmetrical, being shorter and broader on the affected side. There is *scoliosis* of the cervical and upper thoracic spine, with convexity toward the healthy side; lower down, a thoracic scoliosis in the opposite direction; and still lower, a lumbar scoliosis in the same direction as the cervical, the whole spine thus presenting an S-shaped scoliosis. One *sternocleidomastoid muscle* is shorter than the other; it is often reduced to a narrow, firm cord. The *head* is inclined toward the shoulder on the affected side, and is slightly rotated toward the healthy side.

Not to be confounded with the above form of caput obstipum, is the so-called **torticollis spastica,** or **tic rotatoire** of the French, in which there are attacks of clonic or tonic spasm of one M. sternocleidomastoideus, and usually of the retrocervical muscles of the other side—a troublesome form of neurosis.

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## 3. Examination of the Muscles, Bones and Joints of the Thorax

The recognition of fracture of the ribs or of the sternum belongs to surgery. The internist, however, will suspect a *fractured rib* if there be pain on deep inspiration, especially on laughing, sneezing or yawning, after a trauma. If the history of trauma be not obtained, pleurisy may be suspected. The crepitation of rib fragments on auscultation is, however, different from that due to pleurisy, and if a tender spot on a rib be found, an attempt should be made to cause indirect pain at that point by pressure and counter-pressure on the rib in front and behind the suspected lesion and at some distance from it.

In examining for **inflammations** or **tumors** of the muscles and bones of the wall of the thorax, care must be taken, first, to exclude processes originating within the thorax itself, especially an empyema breaking through the thoracic wall (*empyema necessitatis*), due either to pyogenic infection, tuberculosis or actinomycosis. This can easily be ruled out by a carefully taken anamnesis and a thorough physical examination of the lungs and pleura.

Of the processes originating in the bones of the thorax or in the muscles of its wall, some are acute and some are chronic. The *acute processes* include *osteomyelitis* of the clavicle, scapula, ribs and thoracic spine. Among the *chronic processes* may be mentioned, chronic inflammations, especially *tuberculosis* and *syphilis* of the lymph glands, muscles and bones, and *neoplasms*, especially primary sarcoma and enchondroma, and secondary metastatic carcinoma of the bones from primary cancer of the breast, prostate or intestine.

The *diseases of the breast* are easily differentiated from other diseases of the thoracic wall; they have been referred to in Part X.

## 4. Examination of the Muscles, Bones and Joints of the Pelvis

Primary diseases of the pelvic bones and muscles are often overlooked in the beginning, or attributed to other causes, owing to the fact that they are covered to so great an extent by soft parts. The *indirect symptoms* to which such processes may give rise are, therefore, very important in diagnosis. Thus, in obscure disturbances of the bladder and rectum, the possibility of a pelvic tumor growing inward and compressing or displacing the pelvic viscera, should be thought of, and a *vaginal* and *rectal examination* made.

**Tumors originating in the bones** of the upper part of the pelvis, or tumors lower down, growing outward, may give rise to a palpable mass, or may compress the nerves or the blood vessels; thus, in sciatica or in edema of the legs without apparent cause, the possibility of pelvic bone tumor should be thought of. Such tumors may be *osteomata, enchondromata* or *sarcomata.* The latter are particularly prone to cause nervous symptoms; they are usually vascular, and sometimes a bruit is audible over the tumor. Röntgenograms of the pelvis should be made in all obscure cases.

**Tumors of the muscles** of the pelvis most often involve the muscles of the buttock. They are usually *fibromata* or *sarcomata.*

*Dermoid cysts* of the perirectal tissue above the M. levator ani may be confused with other pelvic tumors; very often they are mistaken in women for ovarian tumors, in men for cold abscesses. *Echinococcus cyst* of the periprostatic area is sometimes mistaken for neoplasm.

## 5. Examination of the Muscles, Bones and Joints of the Spine

### (*a*) *Spina bifida and Other Congenital Anomalies*

In the new-born, sessile masses in the middle line are usually associated with *spina bifida*, in which case we may have to deal with (1) a **rachischisis posterior,** in which there is a complete defect in the spine, meninges, and posterior part of the spinal cord; (2) a **myelomeningocele,** in which the spinal cord is closed but is adherent to the dorsal wall of the sac and projects from the canal; or (3) a **pure meningocele,** in which the mass consists of the projecting arachnoid.

More difficult to recognize are the cases of **spina bifida occulta,** in

which there is no external mass. The patients complain of slight motor, sensory or trophic disturbances in the lower extremities. Over the lower part of the back in the middle lines one sees an area of hypertrichosis, the hairs being usually arranged in a crescent, which lies across the region of the spine, with convexity below. On palpation, a defect of the vertebral spines in this area can be made out.

**Congenital tumors of the lumbosacral region** are not uncommon (teratomata, angiomata, sarcomata, fibromata, lipomata, etc.).

At the lower end of the sacrum there is sometimes an **abortive tail.** This may be a *true tail,* containing rudimentary vertebrae; sometimes the appendage does not contain bone. In other cases a *false tail,* due to a lipoma or a fibroma, appears in this region.

### (*b*) *Lumbago*

Pain in the lumbar region of the back is called *lumbago.* It should be remembered that lumbago is not a disease, but, like jaundice, only a symptom that may be due to any one of several different causes. It is probably best to reserve the term for violent pains that set in suddenly, without recognizable cause—the *Hexenschuss* of the Germans, in which case the less severe and more chronic pains of spondylitis, of renal stone, renal tuberculosis, chronic colitis, tabes, etc., are excluded.

Lumbago, so restricted, is believed by some to be *rheumatic* or *gouty* in origin, by others to be always *traumatic,* though the trauma may be very slight.

The lumbar portion of the spine undergoes muscular fixation, and movement of the part is exceedingly painful. When a severe trauma has preceded the lumbago, one must rule out fracture of the spine (x-ray); if no outspoken trauma have preceded, *the cause of lumbago is most often an excessive movement of one of the lateral joints of the spine, causing strain (distortion) of the joint.* Some persons are particularly prone to produce such lesions in themselves. It is probable that many of the cases of lumbago believed to be due to "rheumatism" of the muscles of the back are in reality instances of slight unilateral joint distortion. Careful x-rays of the spine often reveal, however, a spondylitis deformans (*hypertrophic osteo-arthritis*), or a beginning *spondylitis ankylopoietica* (chronic infectious arthritis of the spine) as the cause.

### (*c*) *Trauma Involving the Vertebral Column*

When an *injury of the spine* has occurred, it is important, first of all, to determine whether or not the *spinal cord* or the *spinal nerve roots* have been injured. This necessitates a careful examination of the *motility,* the *sensibility,* and the *vasomotors* of the lower extremities, and the *reflexes* (deep, superficial, pupillary, sphincters). Should a neural dis-

turbance be found, its *exact site* must be determined (see Part XII, Subdivisions I and II). We can then deduce the site of the vertebral injury causing the symptoms, and good röntgenograms will reveal its nature and extent.

Vertebral injuries may cause nerve lesions that are *irreparable,* in which case they consist usually of *total dislocations of the spine* or total dislocations with fracture, or they may cause nerve lesions that are largely *reparable,* in which event they consist usually of *fracture of an arch* of a vertebra or a *compression-fracture* of a vertebra.

If the injury to the spine has not caused any alterations in the form of the spine, or any neural symptom, it must have been either merely a *contusion,* or a strain (*distortion*), or, possibly, *fracture* of a spinous process, or of a transverse process.

### (*d*) *Diseases Involving the Bones and Joints of the Spine*

*Non-traumatic diseases* in the region of the spine may be inflammatory, neoplastic, or metabolic in origin.

Of the *inflammatory diseases of the spine* and its neighborhood, the most important for the internist is undoubtedly **tuberculous spondylitis,** or *caries of the spine,* familiarly known as *Pott's disease.* In the severer forms, tuberculous spondylitis is accompanied by compression myelitis and spastic paraplegia; in the less severe forms, it may be associated with angular deformity of the spine (*gibbus*), or with *cold abscess* pointing in the groin, in one iliac fossa, beneath the muscles of the buttock, on the posterior surface of the thigh, in the back, in the perirectal region, in the neck, or in the posterior wall of the pharynx.

In *young children,* tuberculous spondylitis can sometimes be diagnosed in the absence of either gibbus or cold abscess. In such cases, pain in the back on descending a stairs may be the first symptom, but any neuralgic pains in the occipital region, in the cervical region, in intercostal areas, or in the sciatic region, should make one think of the possibility of a beginning spondylitis. In such cases, the spine should be carefully examined for tender spots, especially for tenderness on the application of a hot sponge, or tenderness on compression of the head or of the shoulders in the long axis of the spine (*Caution!*); x-ray examinations and tuberculin tests may be helpful.

**Neoplasms** or true tumors in the region of the spine may involve the bones of the spine, the muscles in the neighborhood, the meninges, or the spinal cord itself.

If a *carcinoma* has been removed from the breast or from another organ, and months or years later a persistent intercostal neuralgia, or a sciatica develop, one must at once fear a *metastasis in the spine;* or, if, after a severe neuralgia, a mass appears in the region of the spine, or

if a slight deformity of the spine occur with sudden paraplegia, a *malignant neoplasm of the spine* is probable.

*Tumors of the meninges and of the spinal cord,* and their symptoms, are described in Part XII, Subdivision III. Some of these are accessible to surgery, and a most careful examination should be made in every case of suspected tumor in the hope that, if one be found, it can be successfully removed. *Root pains* are usually the first symptom. They are unilateral in the beginning, except perhaps in the region of the cauda equina, where they may be bilaterally symmetrical. In deciding upon the *level* of a tumor involving the spinal cord or the nerve roots it should be remembered, first, that sensory symptoms are more important than motor for level diagnosis, and, second, that as a rule the lesion is a little higher than the symptoms lead one to suspect (see Level Diagnosis, Part XII).

Of the *metabolic diseases* of the spine, the two most important are **rickets** and **osteomalacia.** They lead especially to curvatures of the spine.

### (*e*) *Curvatures of the Spine*

Curvature of the spine is not a disease in itself, but merely a symptom. Any *static disturbance* of the body leads to a compensatory change in the spine, to restore the equilibrium; thus, the shortening of one leg causes obliquity of the pelvis, and, in turn, lateral curvature of the spine. Similarly, a flexion-contracture of the hip joint will tilt the pelvis and cause lateral curvature of the spine. Any *painful condition* such as sciatica will lead to fixation of the pelvis and of the spine, with curvature (*scoliosis ischiadica*). Again, if the muscles whose contractions normally support the spine are weakened, *paralytic curvature* will develop, as in the lumbar lordosis of progressive muscular atrophy, the scoliosis of the Heine-Medin disease, of syringomyelia, and of Friedreich's disease. Again, *retraction of one side of the thorax* after a thickening of the pleura or an empyema, will cause lateral curvature of the spine.

Curvatures may, however, arise from diseases of the spinal column itself; thus *spondylitis* is often a cause of kyphosis or of scoliosis. *Faults of development* of the spine (supernumerary ribs, absence of a rib) may cause scoliosis. In *Paget's disease* and in *acromegaly,* curvatures of the spine also occur.

Ordinary curvatures of the spine, however, are due to causes other than those already mentioned, and they depend chiefly upon softening of the bones of the spine due to early or late *rickets,* or to *osteomalacia.*

The symmetrical, or anteroposterior, curvatures include **kyphosis,** or convexity backward, and **lordosis,** or convexity forward. An asymmetrical or lateral curvature of the spine is known as **scoliosis.**

Observing mothers are often the first to notice the deformity; they bring the child to the physician complaining that "one shoulder is a little higher than the other," or that "one hip projects a little."

Sometimes the spine is abnormally flat (*shoemaker's spine*), or there

may be merely an exaggeration of the normal curves, or, finally, entirely abnormal curvature may be present. Normally, there is a moderate lordosis of the lumbar region and a moderate kyphosis of the thoracic region. Practically, the lateral curvatures, or scolioses, are the most important of the abnormal curvatures. A general practitioner should see to it that he recognizes a scoliosis early and does not neglect its treatment. An excessive lordosis of the lumbar spine in adolescence is often associated with orthostatic albuminuria.

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# 6. Examination of the Muscles, Bones and Joints of the Upper Extremity

## (*a*) *Examination of the Region of the Shoulder*

Fractures and dislocations of the clavicle, acromion, scapula, fractures and dislocations of the shoulder joint, need not detain us, though a knowledge of the diagnostic points in surgical conditions in this region is essential to the internist, in order to avoid the confusion of them with non-surgical diseases of the shoulder-joints.

Among the congenital malformations near the shoulder, a *high position of the scapula* is not uncommon.

**Inflammations** of the *acromioclavicular*, the *sternoclavicular*, and the *shoulder joints*, and inflammations of the *bursae* of this neighborhood, including the *subacromial bursa* and the *subdeltoid bursa*, may be met with. The *subscapular bursa* and the *intertubercular bursa* are extensions of the sac of the shoulder joint, and do not become inflamed except when the joint itself is also inflamed. The *subcoracoid bursa* is very small and clinically unimportant.

The **subdeltoid bursa** is of great importance, however, and gives rise, when inflamed, to a typical disease-picture. It lies between the deltoid muscle and the joint capsule and the humerus, and is sometimes divided into two sacs—an upper, or *bursa subacromialis*, and a lower, or *bursa subdeltoidea proper*.

It is necessary to distinguish an effusion into the subdeltoid bursa from an effusion into the shoulder joint. When the subdeltoid bursa is distended with fluid, the M. deltoideus can, on *inspection*, be seen to be raised from the joint and from the humerus, especially in front and lateralward. The enlargement is most easily recognized if the patient be viewed from behind (over both shoulders), so that the diseased may be compared with the healthy side (Küster). This striking bulging is absent in joint effusion. An extension of the bulging of the deltoid downward at once excludes joint effusion (de Quervain).

When there is a large effusion into the shoulder joint, it causes bulging; but this is usually most marked posteriorly and over the prolongation of the synovial sac along the biceps tendon. On *palpation* in bursal effusion a cushion between the deltoid and the humerus can be felt, and tenderness on pressure is limited to the region of the bursa; in arthritis the tenderness is most marked at the posterior inferior part of the joint.

A *subdeltoid bursitis* may be due to acute infection, to trauma or to tuberculosis. An *inflammation of the shoulder joint* (*omarthritis*) may be due (1) to acute infection (streptococcus, gonococcus, etc.); (2) to chronic infection (tuberculosis, streptococcus, lues), or (3) to trauma, followed by a hypertrophic osteo-arthritis.

It must not be forgotten that a *primary disease of the bone* in the neighborhood of the shoulder joint may simulate either omarthritis or bursitis, but a careful examination will usually differentiate, especially if röntgenograms be made (in two directions, at right angles to one another). *Osteomyelitis, tuberculosis, gumma,* and *sarcoma* are the most common diseases of the bones in this neighborhood.

### (*b*) *Examination of the Elbow and the Forearm*

The elbow may be the site of any one of several *surgical injuries* (fractures, separation of epiphyses, dislocations). These are differentiable from one another on careful *inspection, palpation, functional testing* of the joint, and, above all, *x-ray examination.*

The medical diseases of the region of the elbow include inflammatory processes and neoplasms. **Inflammations of the elbow** and its neighborhood may be acute or chronic. A phlegmon of the forearm may simulate an *acute arthritis of the elbow joint,* but on close examination it will be found that one side of the joint is free, while in acute arthritis the whole circumference of the joint is tender on pressure, the swelling being most marked where the capsule is most superficial (near the head of the radius and on both sides of the triceps tendon).

*Chronic arthritis of the elbow joint* may be due to (1) tuberculosis, (2) lues, or (3) other forms of chronic infectious arthritis. An arthritic involvement is not likely to be confused with simple chronic *bursitis olecrani* or with *epicondylar neuralgia.*

**Inflammations of the muscles** of the upper arm and of the forearm, may be due to (1) *simple infectious myositis,* (2) *gummatous myositis,* (3) *tuberculous myositis,* or (4) *trichiniasis.*

Of the **tumors** of this region, those of intramuscular origin include *angioma* and *sarcoma.* The simple *muscle hernia* due to the bulging of contracted muscle through a defect in the aponeurosis of a muscle, following trauma or congenital defect, should not be mistaken for neoplasm. Similarly, calcification within a muscle following trauma, the so-called *traumatic osteoma,* in reality a circumscribed ossifying myositis, should not be mistaken for tumor; the appearance in röntgenograms is very characteristic.

Tumors originating in the nerves rather than in the muscles can be differentiated from muscle tumors by their position in the course of the nerves and by their spindle shape. They consist usually of *neurofibromata,* more rarely of *sarcomata.*

**Inflammations of the bones** may be *acute* (osteomyelitis) or *chronic* (chronic staphylococcus osteomyelitis, sporotrichosis, tuberculosis, or gumma). The **neoplasms** of the bones found here are most often *myeloid sarcoma;* occasionally other forms of *sarcoma, fibroma* or *enchondroma* may be met with.

### (c) *Examination of the Wrist and Hand*

On examination of the wrist and hand we have to consider especially the bones, the joints and the tendon sheaths (vaginae mucosae).

Knowledge of the effects of **trauma** in this region has been greatly advanced by x-ray examinations. Formerly, an outspoken *Colles' fracture,* with silver-fork *deformity,* was, of course, easily recognized by the dorsoradial deviation of the distal fragment (with retention of freedom of the wrist joint), along with deviation of the styloid process of the radius and the wrist from the axis of the radius. But aside from this, other injuries were diagnosed as strain (*distortion*), or, rarely, as *dislocation* of the wrist. By means of the x-ray, however, a whole series of *other injuries* of this neighborhood have been analyzed, and many of them can now be recognized, even without the help of the x-ray. Among them are the fractures of the radius extending into the wrist joint, fracture of the styloid process of the ulna, fracture of the os naviculare, volar dislocation of the os lunatum, and combinations of the two (intercarpal luxation-fracture). Fractures and dislocations of the metacarpal bones and of the phalanges are easily recognized, with or without x-ray examinations.

The more distinctly medical diseases of this region include the *inflammations* and the *neoplasms.*

Of the **acute inflammations of the wrist joint** and its neighborhood (*cheirarthritis*) we may mention (1) acute arthritis of the wrist due to *acute rheumatic fever,* or to other forms of *acute infectious arthritis,* and (2) acute inflammation of the vaginae mucosae (*tendovaginitis*) secondary to a penetrating wound of a finger, to a bite or other injury, or, sometimes, to metastatic infection.

In *tendovaginitis,* it is chiefly the movement of the fingers that is disturbed, while in *arthritis* of the wrist it is chiefly movements of the hand as a whole that are concerned; moreover, in arthritis there is everywhere tenderness on pressure, while in tendovaginitis only the side affected is tender. Again, traction or compression in the long axis of the extremity is painful in arthritis, not in tendovaginitis. Extension of the inflammatory process in the longitudinal direction is characteristic of tendovaginitis; in arthritis, the inflammation remains limited to the joint region. Sometimes, of course, arthritis and tendovaginitis occur together.

A painful swelling in the region of the long extensor of the thumb, accompanied by crackling on palpation over the tendon and muscle, is the so-called *tendovaginitis crepitans;* it is a croupous inflammation of the vaginae mucosae of the tendon and of the surrounding tissues.

The metacarpal and phalangeal joints are often the site of arthritis. The proximal phalangeal joints, especially, undergo spindle-shaped thickening in chronic infectious arthritis (*arthritis nodosa*).

**Heberden's nodes,** the bony excrescences at the bases of the terminal phalanges, are commonest in hypertrophic osteo-arthritis, though they may occur in other forms of arthritis.

An acute osteomyelitis may involve a metacarpal bone or a phalanx, though it is not common here. A gouty attack, involving the wrist and hand, is a rarity, but it does occur.

Of the **chronic inflammations in and about the wrist,** *chronic infectious arthritis* is very common. If one wrist alone is affected, and no other joints in the body are involved, *tuberculosis of the joint* is probable.

It is easily distinguishable from *tuberculous tendovaginitis,* since in the latter the swelling is only on one side of the wrist, usually the volar side, and is most marked, not at the level of the wrist itself, but proximal and distal therefrom. The fingers are slightly flexed and there is no volar subluxation of the hand as in tuberculous arthritis.

Of the **chronic inflammations of the hand and fingers,** we must keep in mind (1) *tuberculosis of the tendon-sheaths,* especially of the flexor tendons, (2) *gonorrheal tendovaginitis,* (3) the *stenosing tendovaginitis* of de Quervain (radiating pain in the thumb and forearm on use, due to stenosis of the compartment of the tendon sheath for the M. extensor hallucis brevis and M. abductor hallucis longis over the styloid process of the radius), (4) the spindle-shaped swellings of the metacarpal bones or phalanges, due to tuberculosis (*spina ventosa*), or to syphilis (*dactylitis syphilitica*).

Mutilating affections of the bones of the fingers may be due to *leprosy, syringomyelia* (Morvan's disease), or *Raynaud's disease.* Among the *ulcers* of the skin that may extend deep into the tissues may be mentioned *hunterian chancre, lupus,* and *cancer,* especially *x-ray cancer.* The occurrence of nodules due to tuberculosis of the skin in pathologists (*Leichentuberkel*), and in butchers, should be kept in mind.

Of the inflammations of the nail-bed (matrix unguis), especially at the hidden margin of the nail, the commonest forms are *paronychia syphilitica* of secondary syphilis, primary syphilitic chancre, and the severe *panaritia* due to atrophic disturbances in syringomyelia, in Raynaud's disease, and in diabetes.

**Tumors of the hand and fingers** may be benign or malign. Of the former, *lipomata, fibromata, angiomata,* and *chondromata* may be mentioned. Of the latter, *sarcomata* occur chiefly on the fingers; *epitheliomata* on the back of the hand. Before röntgenologists learned how to protect themselves, *röntgen-dermatitis,* leading to epithelioma, was very common. Some of the finest men in the profession have been sacrifices to it.

Certain **conditions resembling neoplasms** should not be mistaken for them. De Quervain mentions (1) ordinary *ganglion,* so common on the back of the wrist, due to gelatinous degeneration of the connective tissue of the capsule of the joint, but known now to be entirely independent of the synovial membrane of the tendon sheaths and of the joints; (2) masses of *tuberculous granulation-tissue* appearing beneath the skin between the tendons as a complication of tuberculosis of the carpal joint (*tuberculomes juxtasynoviaux* of Ollier); (3) *sebaceous cysts* on the back of the hand; and (4) *epithelial cysts* (traumatic or congenital) of the palm.

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# 7. Examination of the Muscles, Bones and Joints of the Lower Extremity

## (a) *Examination of the Hip and Thigh*

In the region of the hip joint, great difficulty may be experienced in differential diagnosis. For this reason the surgeons, especially, have devised methods of examination, including measurements, which are very helpful, and with which every physician should be familiar. For the details of these, text-books of surgical diagnosis, like those of de Quervain and of Johnston, should be consulted. Here only the more salient facts can be referred to.

**Limps.**—If the hip joint be involved, the patient will *limp.* There are several varieties of limping, by no means all of them due to involvement of the hip. They have been carefully analyzed by F. de Quervain.

A limp may be due:

(1) To *shortening* of the lower extremity (more than 1½ cm.)

(2) To *muscular paralysis* from nerve lesion or from dislocation (*paralytic limp*); here, one extremity is not sufficiently supported, and the patient steps forcibly on the affected side, evidently feels no pain in it, but limps on one side in order to place himself more firmly on the affected leg, and, as it were, to

throw the affected leg forward for the next step; this is the form of limp seen in congenital dislocation of the hip, and, if bilateral, a typical waddling gait or duck-walk develops.

(3) To *painless rigidity of one hip joint*, the whole extremity, including one half of the pelvis, being moved forward as one piece, the gluteal fold disappearing on the affected side. Bilateral stiffness of the whole lower extremity is met with in outspoken bilateral coxa vara. The pelvis oscillates around a vertical axis, not around a sagittal axis as in bilateral congenital dislocation.

(4) To *pain* in some one of the joints on the affected side on movement; all the joints of that side undergo muscular fixation. The patient avoids using the affected extremity as a support, and so his body becomes inclined toward the healthy side, a point that distinguishes the painful limp from the limp of painless stiffening, which it otherwise resembles, especially in the absence of the gluteal fold. The limp of *intermittent claudication* (*q. v.*), due to arteriosclerosis, is a painful limp.

**The Hip.**—If after an injury, a dislocation or a fracture of the hip joint be suspected, the *position* and *attitude* of the injured extremity should be closely inspected, for this alone will often give a clue to the nature of the injury. Inspection is followed by careful *measurements* (see Examination of the Bones), to ascertain whether or not there is shortening, and, if so, whether it is supratrochanteric or infratrochanteric.

The *position of the trochanter* is determined by means of the Roser-Nélaton line, or, better, by outlining Bryant's triangle or drawing Shoemaker's line (*q. v.*).

If there is *shortening* that was not present before the injury, a dislocation or a fracture has occurred. If the shortening is supratrochanteric, there has been a dislocation or a fracture of the neck of the femur; if it is infratrochanteric, there has been a fracture below the tip of the trochanter. If the trochanter be abnormally high, it indicates a dislocation or a fracture of the neck. If the trochanter occupy its normal position, there can have been no dislocation, or, if there be one, it must be situated below the trochanter.

The *active movements* of the leg are next examined. If a patient, undressed, lying flat on his back, can lift the injured leg easily, there is no dislocation nor fracture. If he flex the thigh with difficulty, without raising the heel from the bed, an impacted fracture may have occurred, in which event there will be limitation of active medial rotation. If it be necessary to test the *passive movements*, an anesthetic is desirable if the pain be marked.

The diagnosis of the various effects of *trauma* (dislocations, fractures, distortions and contusions) is relatively easy if the anatomical facts be kept in mind and the disturbances of function be carefully analyzed.

The *non-traumatic alterations* in the form of the hip joint are of greater interest to the internist than those just mentioned. I refer to the changes in form that accompany *congenital dislocations* of the hip

and those associated with *coxa vara.* The two are sometimes confused, though if röntgenograms be made this confusion could scarcely occur.

### i. Congenital Dislocation of the Hip

In *congenital dislocation of the hip,* the head of the femur lies above or behind the acetabulum, there is shortening of the line joining the anterior superior iliac spine and the lateral malleolus, and the tip of the trochanter lies abnormally high. There is excessive mobility of the thigh, and the head of the femur can be found in an abnormal position and can be moved backward and forward on the pelvis. There is usually a high grade of lumbar lordosis. In the röntgenogram, the exact position of the head itself, especially, and that of the acetabulum, can be made out. In the anamnesis a history of limping or of waddling from earliest childhood can be obtained.

The abnormal mobility distinguishes congenital dislocation of the hips from *bilateral coxa vara* due to rickety curvature of the femur, as does the x-ray examination. Paralysis of the gluteal muscles from the *Heine-Medin disease* may cause a paralytic limb resembling congenital dislocation, but the anamnesis will reveal the fact that the child walked perfectly well before his attack of poliomyelitis; moreover, the tip of the trochanter is in the normal position, and the x-ray examination shows the head of the femur in the acetabulum.

### ii. Coxa vara

In *coxa vara* dislocation is ruled out by the fact that the head of the femur is in its normal position and the femur is not abnormally mobile on the pelvis, but a clue to the condition is found in the high position of the trochanter, caused by the bending of the neck of the femur.

Kocher distinguishes two forms of coxa vara: (1) *coxa adducta,* in which, for some reason or another, the oblique angle formed by the neck of the femur is diminished and converted into a right angle, or even into an acute angle; and (2) *coxa vara in the narrower sense,* in which the head is bent downward and backward, and undergoes spiral rotation, and the neck of the femur is also displaced backward; when viewed from the trochanter, the neck, otherwise fairly normally placed, is turned backward in the direction of the hands of a clock. These changes in the position of the neck of the femur in coxa vara may be due in childhood to rickets, in later life to the carrying of heavy burdens, or, more rarely, to osteomalacia. The coxa vara of childhood is usually bilateral; that of adults may be either unilateral or bilateral.

The characteristic signs of *coxa adducta* are: (1) anterior position and abnormally high position of the trochanter, (2) limitation of abduction, and (3) (when unilateral) shortening. The signs of *coxa vara in the narrower sense* are: (1)

anterior position and abnormally high position of the trochanter, (2) lateral rotation and limitation of abduction of the thigh, (3) medial rotation and flexion, and (4) (when unilateral) shortening and limping.

Coxa vara has to be distinguished (1) from *congenital dislocation of the hip* (see above); (2) from beginning *coxitis;* (3) from the *effects of trauma.*

### iii. Acute Coxitis

Of the acute inflammations of the hip and its neighborhood, we have to distinguish acute inflammations of the hip joint itself **(coxitis acuta),** (1) from *osteomyelitis* of the shaft of the femur (cautious passive movement possible; local tenderness below trochanter); (2) from *iliac abscess;* (3) from *adenitis* of the femoral or inguinal lymph glands and (4) from acute *phlebitis* of the femoral vein.

If an *acute arthritis* be present it may be due to acute rheumatic fever, to other kinds of infectious arthritis, to luetic arthritis, or to very acute tuberculous coxitis.

### iv. Chronic Coxitis

Of the *chronic infections* of the hip joint by far the most important is *tuberculous coxitis,* the common "hip joint disease" of childhood. In adults *non-tuberculous arthritis* is more common.

In **tuberculous coxitis,** the child begins to show a *painful limp,* the *gluteal fold* disappears, and the muscles of the thigh begin to *atrophy.* Sometimes the child complains of *pain in the knee* rather than in the hip, but examination of the knee-joint reveals nothing abnormal there. On examination of the child lying on its back with the legs straight out, there is obvious *lordosis* of the lumbar spine, permitting the examining hand to be inserted beneath the back. If this lordosis be overcome by strong flexion of the thigh of the healthy side, there will be involuntary flexion of the thigh of the affected side when tuberculous coxitis exists (*Thomas' test*). There is *fixation* of the affected extremity and the pelvis, these parts moving as a whole. Under an anesthetic the muscular rigidity disappears. On testing for *limitation of passive motion,* abduction and rotation are found to be involved earliest, then adduction, and, lastly, extension and flexion.

After the disease has lasted for a time a *cold abscess* may form, pointing most often in front below the anterior superior iliac spine, sometimes, however, lateralward and backward. *Tenderness on pressure* can be elicited at the front of the joint below the middle of Poupart's ligament, and *compression in the long axis* of the femur or from the trochanter is also painful.

*X-ray examination* is helpful, though in the earliest stages of tuberculous coxitis it may leave us in doubt. There is always an osteoporosis due

to disuse. After the disease has advanced and has involved the cartilage and bone, the x-ray findings may be very characteristic.

It goes without saying that a cold abscess due to tuberculous coxitis should never be incised unless the surgeon intends immediately to go on to complete radical operation. If the physician desires to make sure as to the nature of a fluctuating mass supposed to be a cold abscess, he may puncture and aspirate under aseptic precautions. This does no harm.

We have to distinguish tuberculous coxitis (1) from subacute forms of *simple infectious coxitis;* (2) from *chronic infectious arthritis;* (3) from *congenital dislocation* of the hip; (4) from the different forms of *coxa vara;* (5) from *caries of the spine and of the pelvis,* with cold abscess formation; (6) from *peri-appendiceal abscess* and *perinephritic abscess;* (7) from *hydrops of the bursa iliaca;* (8) from *sciatica* and other neuralgias; and (9) from *hysteria* (Brodie's joint).

**Non-tuberculous chronic coxitis** may be either a *coxitis deformans,* which is in reality a part of a hypertrophic osteoarthropathy, a common form of it being the so-called *malum coxae senile,* or it may be a *coxitis chronica ankylopoietica* due to chronic infection with some bacterium other than the tubercle bacillus. Occasionally the hip is involved in a *neuropathic arthropathy* (tabes; syringomyelia).

#### v. Neoplasms of the Hip and Thigh

Of the *neoplasms* of the hip and thigh those involving the muscle include *angioma, fibroma* and *sarcoma* (to be differentiated from *tuberculous myositis, gummatous myositis,* and *muscle hernias*). Those originating in the bone include *cartilaginous exostoses, enchondromata, osteomata,* and *myeloid sarcomata.* Such tumors of the bone must be distinguished from *osteomyelitis* (acute and chronic). A *spontaneous fracture* of the bone may occur in sarcoma.

### (*b*) *Examination of the Knee*

#### i. Effects of Trauma

In the domain of the knee-joint (*articulatio genu*), **trauma** is very common. In falling, the knee often strikes first, and there may be an injury to the *bursa prepatellaris,* to the *patella,* or to the *knee-joint* itself.

An *effusion into the bursa* is easily recognizable from its location and limitations. When there is an **effusion into the knee-joint** itself, the knee cannot be fully flexed, and there is swelling, not in front of, but around the patella, the grooves on both sides of this bone being filled out. Often there is also a transverse swelling above the patella where the joint cavity extends up beneath the tendon of the M. quadriceps. Joint effusion lifts the patella from the condyles of the femur. If pressed with the finger

down upon the bone the firm substratum can be felt when it is reached; if the pressure be taken off again, the patella will once more float. This is sometimes spoken of as *dancing patella,* or as *ballottement* of the patella.

Trauma to the knee-joint may be followed by **loosening of a cartilage** from one of the condyles of the femur (x-ray; palpation); or if there has been a twist of the joint, especially when the thigh has been rotated outward when the leg is fixed, there may be a **loosening and displacement of one meniscus** (semilunar fibrocartilage), usually the medial meniscus. This causes a disturbance of function of the joint formerly described as ***dérangement interne.*** Such an injury is painful. On examination of the joint, there is tenderness on pressure at the point of attachment of the corresponding collateral ligament, or of the anterior insertion of the meniscus on the tibia. On extending the joint, the meniscus may project from the joint-slit and be palpable. Sometimes the meniscus is displaced into the interior of the joint. When a meniscus has been torn off in this way the patient is liable to sudden attacks of *locked joint,* accompanied by severe pain.

If, after an injury, the patient cannot lift the leg when the lower extremity is extended and there is no fracture as proven by the absence of shortening and of pain on compression in the long axis, further examination will reveal either a *fracture of the patella,* a *rupture of the patellar tendon,* or, rarely, a *rupture of the tendon of the M. quadriceps.* Such injuries are much more common than *fracture* of the lower end of the femur or of the upper end of the tibia, though these fractures do sometimes occur, as does also the rare *dislocation* of the knee-joint or of the patella.

### ii. Acute Gonitis

In the acute inflammations of the knee-joint **(gonitis acuta),** the etiology may be that met with in acute arthritis of any of the joints; thus, a *traumatic arthritis* may follow injury, especially if a joint-mouse or a loose meniscus have resulted. Without preceding injury, an acute gonitis is nearly always of infectious nature. *Gonococcal gonitis* is common in young people; indeed "gonorrheal rheumatism" is very likely to localize in one knee-joint, and sometimes it causes suppuration there. In polyarthritis due to *rheumatic fever* or to the *pseudorheumatisms,* the knees are frequently involved.

In all the cases just referred to there is evidence of **effusion into the knee-joint** with floating patella; usually there is also some thickening of the capsule, which can be felt in thin people at its fold of reflection when the affected knee is compared with the healthy knee. Sometimes the cartilages and bones are involved (röntgenograms).

Such acute gonitis must be differentiated (1) from *acute prepatellar bursitis,* (2) from *hydrops intermittens* of the knee, and (3) from *acute osteomyelitis* of the lower end of the femur or of the upper end of the tibia.

### iii. Chronic Gonitis

Many different forms of chronic inflammation of the knee-joint **(gonitis chronica)** are met with clinically. A chronic joint effusion may be due either (1) to *chronic infectious arthritis,* or (2) to *tuberculosis.* In a monarticular affection with chronic serous *effusion* into the knee, especially if there be *thickening of the capsule* palpable at the upper recess of the joint and over the two condyles of the femur (where the synovial membrane is reflected) and definite *local heat,* the condition is probably tuberculous, even though there be no marked *limitation of motion* nor any marked *muscular atrophy* demonstrable in the neighborhood.

When the capsule is markedly and diffusely thickened (so-called **fungous gonitis)** the condition is nearly always *tuberculous;* rarely *gummatous.* This condition has nothing to do with the so-called *villous arthritis,* in which there is crackling of thickened synovial folds as a result of static disturbance. Nor should it be confused with fatty proliferation of the villi (*lipoma arborescens*).

In chronic gonitis, **ankylosis** of the joint is not uncommon. This may follow an acute infectious gonitis (*arthritis chronica ankylopoietica*), or it may be due to *tuberculosis.* Sometimes it follows a hemorrhage into the joint (*hemarthros*).

### iv. Neoplasms and Other Swellings of the Knee, and its Neighborhood

Of the **tumors** in the region of the knee-joint, *lipoma* is the most common. Occasionally, a *sarcoma* of one of the bones is met with, or a *fibroma* or *sarcoma* may originate in the synovial membrane.

Chronic swellings in the neighborhood of the joint, other than neoplasm, are more common. Thus, in front of the joint we may find a swelling due (1) to *chronic bursitis prepatellaris,* (2) to *chronic bursitis pretibialis,* or (3) to *bursitis infrapatellaris profunda* (behind the patellar tendon). Behind the knee-joint, in the popliteal space or poples, swelling due to *aneurism* is not uncommon; its pulsation quickly differentiates it (1) from *distended bursa* here, (2) from *lipoma,* and (3) from *cold abscess.*

## (c) *Sciatica and Other Pains in the Lower Extremity*

When investigating pain in the back of the thigh and leg **(sciatica),** it should be remembered that such pain is only a symptom and not a disease in itself, and that this symptom may be due to any one of several different causes. On examination it is well to proceed systematically. We rule out (1) a *diabetic neuritis* by examination of the urine; (2) the pains of *tabes,* or of *dementia paralytica,* by examination of the reflexes, especially of the pupils, and by the Wassermann test, (3) *sarcoma* of the pelvic bones, or of the gluteal muscles, by palpation, by rectal examination, and by röntgenogram; (4) *chronic osteomyelitis* of the shaft of the femur, by palpation of the bone, and by x-ray examination; (5) *spondylitis* of the

cervical, or of the lumbar spine, and *disease of the sacro-iliac articulation* by testing motion, by lateral compression of the pelvis, and by röntgenogram; (6) *carcinoma* of the rectum, or of the prostate, by rectal examination; (7) *neoplasm of the female genitals,* by vaginal examination; (8) *malum coxae senile,* by x-ray examination of the hip joint; (9) *intermittent claudication,* by inspection of the foot before and after walking, and by palpation of the arteries on the dorsum of the foot and behind the medial malleolus; and (10) *varicose veins,* by inspection and palpation. Only when these several causes for sciatica have been investigated and ruled out dare we assume the existence of a so-called *idiopathic sciatica,* or *simple neuralgia,* of the N. ischiadicus.

In **other neuralgias** of the lower extremity, we may find involvement of the N. femoralis (*anterior crural neuralgia*), of the N. femoris cutaneous lateralis (*meralgia paresthetica*), or of the N. obturatorious (*obturator neuralgia*), a similar thorough investigation should here, also, precede diagnostic conclusions.

**Pain in the foot** may be due to any one of many different causes. *Flat-foot, trauma, arthritis, bursitis, osteomyelitis, tabes, alcoholic neuritis, beginning gangrene* and *gout*—all should be considered. Pain of so-called *gonorrheal heel* is due to an exostosis on the os calcaneum. *Morton's metatarsalgia* may depend upon flat foot, upon exostosis of a metacarpal bone or upon a local arthritis. It involves most often the region of the metatarsophalangeal joint of the fourth toe.

### (*d*) *Tumors and Inflammations of the Muscles and Bones of the Leg*

Of the tumors below the knee, *myeloid sarcoma* of the upper end of the tibia or of the fibula is not uncommon. Sometimes there is marked spindle-shaped enlargement with parchment crackling, and, on auscultation, a bruit is audible over the sarcoma. Such sarcomata have been described in the literature as *bony cysts* or as *bone aneurisms,* since, when incised, they are found to be full of blood. The röntgenogram in such cases is characteristic. *Cartilaginous exostoses* may also occur near the extremities of both the tibia and the fibula.

### (*e*) *Examination of the Ankle and Foot*

Of the inflammations of the bones here, *acute osteomyelitis* is easily recognized, but chronic inflammations may give rise to difficulties in diagnosis. A careful examination, together with röntgenograms, will, however, usually differentiate *chronic staphylomycotic osteomyelitis* from *syphilitic periostitis,* from *gummatous osteitis,* and from *tuberculosis.*

In the **ankle joint** (articulatio talocruralis) and foot, aside from *trauma* causing contusion, distortion, fracture or dislocation, we have to consider chiefly *inflammations, deformities* and *neoplasms.*

Acute inflammation of the joints is very common **(podarthritis).** The inflammation may involve the ankle joint proper (*articulatio talocruralis*) or the intertarsal joints (*articulationes intertarseae*), or the transverse joint of the tarsus (*articulatio tarsi transversa* [*Choparti*]).

Chronic inflammations of these joints, as in the joints elsewhere, may be due to chronic infectious arthritis, to tuberculosis, or to lues, and the same considerations that we have found useful in differentiation higher up also apply here.

The pain due to inflammation of the *bursa tendinis calcanei* (*Achilles*), often called **achillodynia,** should not be mistaken for a beginning tuberculosis.

An acute arthritis of the tarsal joints, and especially an acute arthritis of the metacarpophalangeal joint of the great toe, occurring in middle life or later, is very often due to **gout.**

An acute gouty attack, however, should not be confused with acute inflammation of intermetatarsophalangeal bursa associated with **hallux valgus** (*bunion*), nor with the pain of beginning *gangrene.*

Of the **deformities of the foot,** *flat-foot* (*pes valgus*), often combined with *pes varus,* is perhaps the most important clinically, though *club foot* (congenital or acquired) is also not uncommon.

In *pes valgus* the os calcaneum is turned lateralward, so that, instead of standing in a line continuous with the axis of the leg, it is seen, when viewed from behind, to form an obtuse angle with it lateralward. When, in addition, the arch of the foot has fallen and the anterior part of the foot is abducted at Chopart's transverse joint of the tarsus so that its axis is directed lateralward as regards a line drawn perpendicular to a line uniting the malleoli, we have **typical flat-foot**; on making a print of the sole of the foot with the aid of powder, the well-known form of foot-print of flat-foot is obtained.

Although physicians may well be expected to be familiar with flat-foot and the various painful symptoms to which it may give rise, it is surprising how often the condition is, in practice, overlooked. Pains in the feet, in the calves, in the sciatic region, and in the several joints of the lower extremities may be due to flat-foot. Morton's metatarsalgia is, in some cases, the result of flat-foot.

**Club foot,** including talipes varus and talipes equinovarus, may be either congenital or acquired, the acquired form usually following the Heine-Medin disease or other paralytic disorder (*paralytic club foot*). Club foot may be associated either with flaccid or with spastic paralysis, in the latter case usually with one of the cerebral palsies of children.

In the toes, *hallux valgus,* or **bunion,** is due to the wearing of improper shoes. **Hammer toe** may be due to the same cause, or it may be congenital.

**Tumors of the foot** are not very common. *Sarcoma* of the os calcaneum may occur and may be confused with caries. *Lipoma* and *cavernous angioma* are met with sometimes in the tarsal or metatarsal region.

In the toes, multiple *chondromata* occurs, just as in the fingers. Sometimes one of the toe nails is gradually lifted by a *subungual exostosis* or by a *fibroma*. It is not likely that the "proud-flesh" due to *ingrowing toe nail* will be mistaken for tumor.

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# Part XI

Section II

SPECIAL DIAGNOSIS OF THE PRINCIPAL DISEASES OF THE MUSCLES, BONES AND JOINTS

## A. Special Diagnosis of Diseases of the Muscles, Fascia, Bursae and Vaginae mucosae

These may be conveniently subdivided into:

I. The congenital myopathies.
II. Myopathies due to primary atrophy (the muscular dystrophies).
III. The neuropathic myopathies.
IV. Myopathies due to rupture of the perimysium (muscle hernias).
V. The inflammatory myopathies.
VI. The parasitic myopathies.
VII. The neoplastic myopathies.
VIII. Diseases of the bursae and of the vaginae mucosae.

Many of these have been sufficiently described under methods of examination in Part XI, Subdivision I. The muscular dystrophies, the progressive muscular atrophies, myasthenia gravis, and the various hyperkinetic disturbances will be described, for the sake of convenience, in Part XII (Diseases of the Nervous System).

Here we shall consider only certain more important diseases of the muscles that concern the general practitioner.

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## 1. The Congenital Myopathies

These consist in the main of defects, that is, absence of the whole, or of part, of a muscle.

The muscular defects of greater importance are those that involve, (1) the M. pectoralis, (2) the M. trapezius, (3) the M. serratus anterior, and (4) the M. quadriceps femoris.

These muscular defects are easily recognized by inspection and palpation of the region of the muscle, and, more especially, by functional tests (see Examination of Motility, Part XII).

## 2. Myopathies Due to Primary Atrophy

(*The Muscular Dystrophies*)

See Part XII, Subdivision III.

## 3. The Neuropathic Myopathies

These include: (a) the muscular atrophies due to lower motor neurone lesions, (b) the muscular atrophies due to disuse, (c) the reflex muscular atrophies, including the arthrogenic atrophies, (d) myasthenia gravis, and (e) the hyperkinetic disturbances. They are described in Part XII, Subdivision III.

## 4. Myopathies Due to Rupture of the Perimysium

**Hernia** of a muscle, due to a defect in the aponeurosis that permits a mass of muscle to bulge through it on contraction, may follow trauma; but it often

appears to be due to congenital defect, especially when bilateral. Such hernias are very characteristic in form. They appear, when the muscle contracts, as a transverse mass, and disappear again when the muscle is relaxed.

In the upper extremity they are most common in the M. biceps brachii. In the lower extremity, they occur most frequently in muscles that have to undergo sudden and severe contraction, as, for example, in the adductors of the thigh in men that ride on horseback.

*Rider's bone* is prone to occur in the same muscles.

## 5. The Inflammatory Myopathies

(*Myositis*)

Under this heading we shall include (a) myalgia, (b) the different forms of myositis proper.

### (*a*) *Myalgia*

(*Muscular Rheumatism; Fibrositis*)

**Occurrence.**—Pain in the muscles is often spoken of as "muscular rheumatism," though the term myalgia is a better one. It may interfere with the function of the muscles, and even cause contractures, though no definite thickening like that of myositis can be made out on palpation. It is usually due to cold, this "rheumatic myalgia" being kept separate from the muscular pains due to trauma, to lead-poisoning, or to gout.

The pathogenesis of these myalgias is not known. Some hold the view that the white fibrous tissue is chiefly affected (fibrositis). Later on it may turn out that the "muscular rheumatisms" are in reality mild forms of myositis rheumatica, or neuralgias of the sensory nerve fibers in the muscles.

*Lumbago* is usually classified among the myalgias, but, as a rule, it is rather a distortion of one of the lateral joints of the spine, due to a sudden movement when the joint has not been prepared for it by preliminary fixation.

**Symptoms.**—Pain is the chief symptom, sometimes well localized, sometimes diffuse. The intensity may be extreme. Myalgia may be acute, subacute or chronic. In the acute cases the affected muscles are tender and pressure on them causes reflex contraction. The muscles at rest are hypertonic and sometimes a little swollen. The skin over the affected muscles may be warmer than elsewhere. According to the part affected, different names are used; thus, ordinary "stiff neck" is known as *cervical myalgia,* pain in the lower back as *lumbago,* or *lumbar myalgia,* pain in the scalp muscles as *myalgia capitis,* or *cephalodynia;* other muscles may be the seat of the disease (*myalgia intercostalis,* or *pleurodynia, myalgia pectoralis, abdominalis,* etc.). The terms *scapulodynia, omodynia,* and *dorsodynia* also refer to local myalgias.

**Diagnosis.**—One must make sure that osteomyelitis and arthritis can be excluded. Especially in cases of lumbago, spondylitis lumbalis and relaxation of the sacroiliac joint should be looked for before deciding on a diagnosis of either distortion of a lateral joint of the spine or a myalgia. Definite myositis should also be ruled out. In pleurodynia the condition must be differentiated from pleurisy and from intercostal neuralgia. Neuritis and neuralgias can usually be differentiated by examining the pressure-points corresponding to the nerves; the pain, too, is paroxysmal and more circumscribed.

## (*b*) *Myositis*

**Definition.**—The term myositis is applied to any inflammation of a voluntary muscle or group of muscles.

Besides (i) the local forms of myositis, certain general forms are now recognized, including (ii) the different forms of polymyositis, and (iii) progressive ossifying myositis.

### i. Local Myositis

This may occur as a complication of acute articular rheumatism, and is then known as "rheumatic myositis." In the acute stage the inflammatory exudate in the muscle can be felt as a firm mass. Later on this may be followed by the formation of scar tissue (chronic myositis) or by atrophy of the muscle.

There is a *gonorrheal myositis,* which is not uncommon in association with gonorrheal arthritis. The muscles near the affected joints are most often affected.

Occasionally a *luetic myositis* is met with, in the form of an infiltrating inflammation, or of a gumma.

The so-called *myositis fibrosa* is an end-stage of various forms of acute myositis (infectious, traumatic, parasitic). Local ossification of muscle may occur occasionally; thus soldiers sometimes show ossification of the deltoid muscle where the butt of the gun strikes it; equestrians may suffer from ossification of the adductor magnus muscle in the thigh, and after any injury, involving both bone and muscle, periosteal elements may be displaced into the muscle-substance and be followed by formation of bone (*muscle-osteoma, myositis ossificans circumscripta*).

Abscess in muscle, or suppurative myositis (*myositis purulenta*), is usually a part of a general sepsis. In Japan it not infrequently occurs as a special form of infectious myositis, in which Miyake has found the *staphylococcus pyogenes aureus,* the process involving either one or many muscles.

### ii. Polymyositis

In this disease many muscles of the body are simultaneously affected. There are several clinical forms, including (a) dermatomyositis, (b) hemorrhagic polymyositis, (c) polymyositis with erythema multiforme, and (d) neuromyositis.

#### *1. Dermatomyositis*

**Definition.**—A febrile disease, associated with violent pains, and with palpable swellings in the muscles, with inflammations of the skin, and with edema.

**Symptoms.**—It is a rare but a serious disease, half the cases ending fatally. The onset may be sudden or insidious, with stiffness in the limbs and rheumatoid pains; later, fever, severe muscular pains develop, along with edemas and with inflammations of the skin, especially of the skin over the larger muscle masses. With each exacerbation new muscle groups become affected. The disease may continue for weeks or months. The spleen is often palpable. Albuminuria is common. The joints are unaffected. Full details will be found in the careful paper by Steiner.

**Diagnosis.**—A careful consideration of the anamnesis and of the physical findings will usually permit one to arrive at an accurate diagnosis. The disease must be differentiated (1) from *trichinosis* (preceding gastrointestinal symptoms; eosinophilia; histology of excised particle of muscle; trichina embryos in blood; anamnesis); (2) from *septic myositis* (blood culture).

A **chronic dermatomyositis** has been described (Schultze; Dietschy). It may lead to muscular atrophy and to sclerodermatous changes in the skin and face. In one case there were fistulae leading to the insertions of the muscles, and from these masses of carbonate of lime were discharged.

#### *2. Polymyositis hemorrhagica*

This rare disease usually follows tonsillitis, and may be associated with myocardial involvement (tachycardia, arrhythmia, myocardial insufficiency). It resembles acute dermatomyositis in its general features, but is characterized by the formation of hemorrhagic foci in and between the muscles. The disease often ends fatally; in six out of ten cases collected by Thayer death occurred.

#### *3. Polymyositis with Erythema multiforme*

The cutaneous affection presents the usual appearances of erythema multiforme and may dominate the clinical picture, though, on careful examination, painful nodules in the muscles can be felt, and the use of the limbs is restricted. In these cases, the joints may also be involved. The disease is usually benign, in marked

contrast with the forms of polymyositis described above. The patient studied by Ricketts and the writer recovered.

#### *4. Neuromyositis*

In this form, first described by H. Senator, acute myositis is associated with acute polyneuritis. The symptoms are those of the muscular and the neural disease combined.

### iii. Progressive Ossifying Myositis

*(Myositis ossificans progressiva multiplex; Hyperplasia fascialis ossificans progressiva)*

**Definition.**—A rare disease in which the muscles of the limbs and of the trunk undergo a progressive ossification.

**Etiology.**—The cause of the disease is entirely unknown. It is interesting that it appears most often in persons that show certain congenital malformations, especially microdactylism of the thumbs and the great toes.

**Symptoms.**—At onset, the muscles of the neck, shoulder or back are most often affected. They become swollen and painful, and the condition may be regarded at first as "muscular rheumatism." The skin over the affected muscles may be reddened, and small nodules come and go in the muscles. Gradually the muscles grow stiff and firm, and later assume a bonelike consistence (ossification). The process extends to the other muscles of the trunk, neck, face and extremities, eventually involving most of the skeletal musculature. The deposits show well in röntgenograms, in which they may be seen to involve not only the muscles, but also the fasciae, tendons, ligaments, and subcutaneous tissues. In the worst cases the body becomes rigid, the arms being fixed in the shoulder joints and the lower jaw immobilized, so that a tube may have to be passed through a hole due to an absent tooth in order to introduce food into the mouth.

The process is not limited to calcification, but consists of actual bone-formation, as histological studies show. Some of the patients show infantile testes or ovaries, and some of them have abnormally short limbs and great toes, indicating an abnormal development.

**Diagnosis.**—Difficulty is experienced only at the beginning; later, palpation and x-ray examinations make the condition clear.

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## 6. The Parasitic Myopathies

These include, (1) trichiniasis, (2) echinococcus of muscle, (3) cysticercus of muscle. These conditions have been described in connection with the respective parasites (*q. v.*).

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## 7. The Neoplastic Myopathies

(*Tumors of Muscle*)

Tumors of muscle may be benign or malignant. The *benign tumors* include lipomata, fibromata, and osteomata. The *malignant tumors* include, as primary tumors, angiomata and sarcomata, and sometimes, as a secondary tumor, carcinoma. Tumors of muscles should not be confused with *myositic indurations, tuberculosis, gumma,* or *parasitic invasions.*

**Lipoma.**—This is uncommon in muscle, though it is sometimes met with in the tongue and in the muscles of the trunk and extremities.

**Fibroma.**—This may occur in any muscle, and, while simple in itself, it should be remembered that a sarcoma may be taken to be a soft fibroma.

**Osteoma.**—Osteoma of muscle is rarely a true tumor; more often it is a localized ossifying myositis of traumatic origin. It is probable that in such cases the periosteum is injured and osteoblasts wander into the muscular tissue. It may be that the "Charlie-horse," which causes induration of the muscles of the thigh and limping in athletes, may be a simple myositis, or, sometimes, a localized ossifying myositis. As a rule, it clears up with temporary rest and baking.

**Angioma.**—Angioma is a rather common tumor of muscle, and is sometimes described as a *blood-cyst*. On account of its vascularity, if it occur in a muscle of an extremity, it diminishes in size when the limb is elevated, and fills when the limb is in a dependent position. Sometimes a *bruit* is audible with the stethoscope over the tumor. It is a relatively benign tumor, often existing a long time without harm to its carrier. Attacks of acute swelling due to thrombosis may occur in a cavernous angioma. The tumor is often mistaken for sarcoma or for tuberculosis of the muscle.

**Sarcoma.**—Sarcoma of muscle is far less common than sarcoma of bone, but, unfortunately, occurs with some frequency; thus, in the gluteal muscles, it may be a cause of sciatica. Sarcoma of the muscles of the neck is not uncommon. The tumor usually arises in the aponeurosis of the muscle or the intermuscular connective tissue. These tumors grow rapidly and soon show signs of malignancy.

**Carcinoma.**—Primary carcinoma of muscle never occurs. Secondary carcinoma may involve the muscles either by extension or metastasis, though metastases here are exceedingly rare—much rarer than in bone.

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## 8. Diseases of the Bursae and of the Vaginae mucosae

These consist chiefly of acute or chronic inflammation (*bursitis,* and *vaginitis* or *tendosynovitis*).

About the shoulder, the *bursa subdeltoidea* is often involved. The differentiation of **bursitis** here from omarthritis has been described above (see Methods of Examination). The *bursa subacromialis* is also sometimes the seat of inflammation, as is the *bursa subcutanea olecrani,* the *bursa subtendinea olecrani,* and the *bursa subcutanea epicondyli humeri* of each side. Inflammations of the latter bursa are often erroneously thought to indicate involvement of the underlying bone.

In the wrist and palm of the hand, **vaginitis** or **tendovaginitis** may be a very serious inflammation, especially if the inflammation be accompanied by a purulent exudate. A stiff hand, or stiffness of the fingers, too often results. The diagnosis has already been described. Tendovaginitis on the *dorsum of the wrist and hand* is less common. In chronic polyarthritis, infection of the *intermetacarpal bursae* is a frequent complication. In the lower extremity, the commonest bursal inflammation is **housemaid's knee** (*bursa prepatellaris*). Its clinical features have been described under methods of examination.

The *pretibial bursa*, and the bursa connected with the *flexors of the thigh* at the knee, may also be the seat of inflammation. The achillodynia due to inflammation either of the *B. subcutanea calcanea*, or of the *B. tendinis calcanei Achillis*, has also been referred to.

*Tendovaginitis of the foot* may occur, similar to the tendovaginitis described for the hand.

For references, see page 37 and 46.

## B. Special Diagnosis of Diseases of the Bones (The Osteopathies)

These may be conveniently subdivided as follows:

I. The congenital osteopathies.
II. The degenerative, the toxic, and the endocrinopathic osteopathies.
III. The osteopathies of circulatory origin.
IV. The inflammatory osteopathies.
V. The neuropathic osteopathies.
VI. The parasitic osteopathies.
VII. The neoplastic osteopathies.

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# 1. The Congenital Osteopathies

Under this heading we include, (a) congenital absence of bone (bone defect), (b) the congenitally high scapula, (c) cervical rib, (d) multiple cartilaginous exostoses, (e) dental cysts, and multilocular cystoma of the jaw.

## (*a*) *Congenital Absence of Bone* (*Bone Defect*)

Such defect is usually due to intra-uterine injury of the fetus. Part of an extremity may be lacking. Sometimes a single bone is absent. We may give three examples: (i) fibular defect, (ii) spina bifida, and (iii) hereditary cranioclavicular dysostosis.

### i. Fibular Defect

When the fibula is congenitally absent, there is an outspoken flexed position to the foot (*talipes valgus*), associated with shortening of the extremity and curvature of the tibia forward and medialward. On palpation, the lateral malleolus cannot be found. Often, over the tibia, a longitudinal scar is visible.

The anomaly is frequently bilateral. Sometimes one or more toes are lacking on the lateral side of the foot. Volkmann's subluxation of the foot lateralward is due to fibular defect.

On x-ray examination, one can easily determine whether all or only a part of the fibula is absent.

Röntgenography is the most satisfactory method of investigating bone-defects of all sorts.

### ii. Spina bifida

This has already been referred to under Methods of Examination (*q. v.*).

### iii. Hereditary Cranioclavicular Dysostosis

(*Dysostose cléido-cranienne héréditaire*)

This remarkable syndrome was first described by Marie and Sainton. It is a congenital hereditary malformation characterized by (1) an exaggerated development of the transverse diameter of the skull coincident with a delay in the ossification of the fontanelles, (2) an aplasia of the clavicles, each clavicle being represented by fragments of bone at its extremities connected by a fibrous cord, and (3) the hereditary transmission of the anomalies. The aplasia of the clavicles permits an exaggerated mobility of the shoulders and diminishes the force on elevation of the arm.

## (*b*) *Congenitally High Scapula*

This depends usually upon bony union of the scapula with the cervical spine, though conditions resembling it may be due to muscular anomalies without bony abnormality. Röntgenograms clearly reveal the condition.

This malformation is known as "Sprengel's deformity."

### (c) *Cervical Rib*

**Occurrence.**—A cervical rib may be unilateral or bilateral, and, in its development, it may vary from a very short stump to a long rib. It is often palpable, on one or both sides, in the supraclavicular fossa.

**Symptoms.**—Because it often raises the subclavian artery, the unusual pulsation palpable may give rise to a suspicion of aneurism, and, indeed, aneurism occasionally complicates cervical rib.

Clinically, cervical ribs are often associated with severe *neuralgic pains* in the domain of distribution of the lower part of the brachial plexus, and the nerve strands may be sufficiently injured to cause anesthesias and muscular atrophies. The writer has reported interesting nerve lesions that resulted from a cervical rib in his own case.

In some instances *syringomyelia* is associated with cervical rib. When there are pupillary disturbances, anesthesias, or severe neuralgias, it may

Fig. 495.—Multiple Congenital Osteochondromata in a Patient with Muscular Dystrophy. Note Tumors on the Humeri and the Characteristic Overgrowth of the Radii. (After T. R. Boggs.)

be difficult to decide whether or not syringomyelia coexists. In my own case there was a *dissociation of cutaneous sensation* (loss of tactile and thermal with retention of pain sense), but it was not of the syringomyelic type (loss of pain and thermal sense with retention of tactile sensation). It is probable that compression of the nerves distal from the cord, when it gives rise to dissociation, will yield anesthesias of a different type from those characteristic of syringomyelic dissociation (*q. v.*).

The cases of cervical rib have been collected and carefully analyzed by W. W. Keen. X-ray will often reveal bilateral cervical rib when only one is palpable, and even when no rib is palpable, the presence of a rib may be easily demonstrable in the röntgenogram. A palpable cervical rib may be visible on inspection as a bony projection in the supraclavicular fossa.

Fig. 496. — Röntgenogram of Knee in Case of Multiple Congenital Osteochondromata. (After T. R. Boggs, J. H. H. Bull.)

Numerical variations of the vertebrae and ribs are not at all uncommon, as careful analysis of röntgenograms will reveal.

### (*d*) *Multiple Cartilaginous Exostoses*

A condition is occasionally observed in which cartilaginous and bony growths of variable size and shape appear in symmetrical distribution on the bones of the trunk and of the extremities, especially at points where ossification normally occurs late. They may lead to marked deformities and to limitation of movement. Owing to pressure upon nerves, or upon the spinal cord, they may cause severe pains or paralyses. The course of the disorder is usually progressive. The disease is hereditary and can often be followed through several generations. T. R. Boggs has made a careful study of the affection.

### (*e*) *Dental Cysts and Multilocular Cystoma of the Jaw*

These have been described in Methods of Examination.

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NOTE.—See also references under Forms of Thorax in Part V.

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## 2. Degenerative, Toxic and Endocrinopathic Osteopathies

Under this heading we shall describe (a) osteoporosis or bone atrophy, (b) phosphorus necrosis, (c) rickets, (d) achondroplasia, (e) osteopsathyrosis and osteogenesis imperfecta, (f) osteomalacia, (g) Marie's disease, (h) acromegaly, gigantism, dwarfism and infantilism, (i) leontiasis ossea, and (j) oxycephaly.

### (*a*) *Osteoporosis*

When, for any reason, the muscles of a part are kept at rest for any length of time, the bones beneath lose much of their calcium and become abnormally

transparent on x-ray examination (osteoporosis). In fractures of bone, and in all forms of arthritis, such osteoporosis of disuse occurs. Recently another form of osteoporosis, known as **acute bone atrophy** has been described. It has been referred to under Examination of the Joints.

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### (*b*) *Phosphorus Necrosis of the Jaw*

This has been described under Methods of Examination of the Bones, and has also been mentioned in connection with phosphorus poisoning under diseases of the liver (*q. v.*).

### (*c*) *Rickets*

### (*Rachitis*)

**Definition.**—A constitutional or metabolic disease, of unknown etiology, leading to visceral changes, to changes in the muscles and tendons, and to characteristic skeletal changes that arise chiefly at the periods when the skeleton is developing most rapidly (first two years of life; puberty).

**Etiology.**—The disease appears to be independent of climate, though it is rare in the tropics, at high altitudes, and in northerly regions. It is, however, an exquisitely hereditary disease; thus, a woman who has had two husbands, one rickety and the other healthy, may have many rickety children by the one husband and entirely healthy children by the other. The sexes are equally affected.

Bad hygienic conditions (impure air, poor food, lack of sunlight and exercise) undoubtedly favor the development of the disease. Rickets is much more prevalent among the poor, but it may occur in wealthy families. Recently the question of a relation to the vitamines of the foods has been raised. Thus, rickets is common in children fed on condensed milk, on proprietary foods, and on foods rich in carbohydrates. According to Cheadle, an examination of the diets of rickety children usually reveals a deficiency of animal fat and proteins. At the zoölogical gardens in London the lions' cubs all died of rickets until, at Bland Sutton's suggestion, milk, pounded bones and cod-liver oil were added to the meat diet.

The relation of rickets to lues has been much discussed, and the question is still open, but rickets can certainly occur independently of lues. The frequent association of rickets with bronchopneumonia, with tuberculosis and with chronic diseases of the skin is well known.

**Symptoms.**—Though the disease must be regarded as a general disturbance of metabolism, the skeletal changes dominate the clinical picture. These consist of (1) softening of the bones, with low content in lime salts, leading to abnormal curvatures; (2) loss of bony substance; (3) thickenings due to deposits upon the bones or to swelling of the epiphyses and (4) disturbance in the longitudinal growth of the bones.

Changes in the *skull* may occur as early as the third or fourth month of life. The flat bones of the skull are thinner and softer than normal, so that they can be dented with the finger tip, like felt or paste-board (*craniotabes*). This may be especially marked over the occipital bone. Sometimes circumscribed softening can be made out in the bones of the skull; over such depressed atrophic areas of bone parchment-crackling is elicitable on pressure with the finger.

Toward the end of the first year thickenings and bulgings appear on the frontal and the parietal bones, giving rise to the prominent forehead and the parietal bosses of the disease. If both the occiput and the frontal bone are flattened by these hyperostoses, the square head of rickets (*caput quadratum*) arises, causing a pathological brachycephaly. This square cranium, with broad forehead and prominent frontal eminences is sometimes mistaken for hydrocephalus. If the parietal bones are especially thickened, the so-called *caput natiforme* arises. The *fonticulus frontalis* does not close until late, often remaining open until the third or fourth year. A *systolic brain murmur* may be audible over this fontanelle; it is commoner in rickets than in other conditions, but it is by no means pathognomonic. The *skin* over the forehead is thin, and the subcutaneous *veins* are dilated. Rickety children tend to sweat about the forehead; at night they rub their heads on the pillow so that over the occiput the hair may be very thin. In many children the *maxilla* is changed so that the palatal arch is high, resembling a gothic arch in shape; this may narrow the nasal passages and interfere with respiration. An abnormal position of the permanent *teeth* may follow changes in the shape of the alveolar processes. Dentition is nearly always markedly delayed, and the teeth, when they appear, are often small (microdontia) and deformed.

Fig. 497.—Rachitic Skull —Case in the Basler Kinderspital. (After R. Bing, "Handb. d. inn. Med.," published by J. Springer, Berlin.)

The changes in the *thorax* are important; the *rickety rosary* arises from thickening at the junction of the ribs with their cartilages. Softening of the ribs may lead to marked deformations of the thorax, similar to those met with in obstruction to the breathing from adenoids and enlarged tonsils (curving outward of the margin of the lower aperture of the thorax;

vertical grooves on each side of the sternum; horizontal groove at the level of the xiphoid, or "Harrison's groove"; pectus carinatum, or pigeon breast). In the *spine,* rickety children often exhibit a kyphosis or a kyphoscoliosis.

The deformations of the *bony pelvis* in girls may be of the greatest importance in later life, interfering with child-birth because of diminution of the pubosacral diameter (see Textbooks of Obstetrics).

In the *arms* and *legs,* the thickenings of the epiphyses just proximal from the wrist and ankle are highly characteristic. In addition, the long bones of the forearms and of the legs become curved through muscular contractions, or through the influence of gravity; thus arise bow-legs and knock-knees (**O**-legs and **X**-legs). Flat-foot may be due to rickets and retard walking. Children with a mild grade of rickets may have abnormally fragile bones, with frequent fractures; and "green-stick" fracture is not uncommon, on account of the softening of the bones.

The disease usually reaches its acme before the end of the second year of life, and then quickly recedes. Occasionally the most active stage is met with in the third or fourth year of life. Such cases, and cases that appear, or recur, at the time of puberty, are spoken of as "late" rickets (*rachitis tarda*). In the late forms, *coxa vara* (with high position of the trochanter, shortening of the leg, with limitation of abduction, and atrophy of the muscles of the gluteal and femoral regions) is common, as is also *genu valgum, flat-foot* and *spinal curvature.* Of late years much more attention has been paid to adolescent rickets than formerly (Hutinel, Tobler).

In rickets the *muscles* are loose and poorly developed, so that greater excursions of the *joints* are possible than in normal persons ("double-jointed" people).

As regards the *nervous system,* rickety children are often depressed or apathetic, but not necessarily intellectually backward. The association of rickets with the *spasmophile diathesis* (laryngospasm, eclampsia) has often been noted. Many of these children undoubtedly suffer from *tetany,* due to parathyroid insufficiency.

Osler emphasizes a **triad of symptoms** to which Jenner first called attention: (1) a *diffuse soreness* of the body; (2) slight *fever* (100°-101.5° F.), with nocturnal restlessness; and (3) *profuse sweating,* especially about the head and neck, the pillow often being found soaked with perspiration in the morning.

Rickety children are prone to suffer from *digestive disturbances* and atony of the abdominal muscles (*pot-belly*). The *spleen* and *lymph glands* are often enlarged, especially if anemia coëxist; there is then, usually, a moderate *leukocytosis* (Morse). *Bronchitis* and *bronchopneumonia* are common complications, and are often fatal.

A résumé of the **chemical studies** on rickets will be found in H. G. Wells' Chemical Pathology. Chemical studies of the bones show a marked diminution in the inorganic salts, but the proportions of the different salts present at first seemed to be the same as in normal bone. Later studies show a relative increase of water and magnesium (Gassmann). For some cause or another, there is a failure on the part of the osteoid tissues to calcify. Various reasons have been assigned: (1) an excess of acid in the tissues (acid theory); (2) insufficient lime in the food. Neither view is sustained by the facts (Stöltzner; Pfaundler). The infectious theory and the nervous theory also lack support. Attempts have been made to hold faulty function of the adrenals or of the parathyroids responsible for rickets, but thus far they have not been convincing.

Two views are at present current: (1) some fault in the osteoid tissue which prevents it from taking salts from the blood (Stöltzner), and (2) excessive loss of calcium through the intestine (Dibbelt; Schabad). The pathogenesis is still obscure.

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### (*d*) *Achondroplasia*

(*Chondrodystrophia fetalis, formerly known as Fetal Cretinism, or as Fetal Rickets*)

**Definition.**—A developmental disturbance of the skeleton occurring during fetal life, of unknown etiology, characterized by micromelia, and

Fig. 498.—Adult Achondroplasia. On the Left an Achondroplastic of 41 Years Whose Height Is 112 cm. On the Right an Achondroplasic of 18 Years Whose Height Is 107½ cm. In the Middle a Normal Child of 8 Years Whose Height (116 cm.) Is Intermediate Between that of the Two Achondroplasics. Note in the Achondroplasics the Short Limbs, the Long Trunk, and the Relatively Low Position of the Umbilicus. (After P. Marie, "Exposé des Titres et Travaux Scientifiques," published by Masson et Cie, Paris.)

trident hand, and associated with a normal development of the genital organs and of the brain and intelligence.

**Symptoms.**—The malformation is congenital, and is relatively rare. Many of those affected die when young, but others live to a good old age. In the *skull* there is an enlargement (resembling hydrocephalus), depression of the root of the nose, and prognathism. The *extremities* are very

short (*micromelia*), owing to premature closure of the epiphyses; the curves of the bones of the extremities are exaggerated. The *trunk*, on the other hand, may be normal in length, though the ends of the ribs are thickened. The middle point of the body stature lies above the umbilicus.

Fig. 499.—Hands of an Adult Case of Achondroplasia. The Four Fingers Are All of Almost Equal Length; the Middle and Ring Finger are Together at the Base and Diverge at Their Extremities—Trident Hand. (After P. Marie, "Exposé des Titres et Travaux Scientifiques," published by Masson et Cie, London.)

The appearance of the *hands* and *fingers* is very characteristic. The fingers, being about equal in length and thickened, project in a radial arrangement from the wrist, like the spokes of a wheel. Often the middle and the ring finger tend to become separated from one another, so that the digits form three groups, (1) the thumb, (2) the index and middle finger, and (3) the ring and little finger. This is the well-known *trident hand.*

Fig. 500.—Chondrodystrophic Dwarf. (Med. Service, J. H. H.)

There is marked lumbar lordosis with projecting abdomen. The subcutaneous fat is abundant; the skin is smooth; and the hair is normally developed and distributed. The intelligence is usually good. Other congenital malformations may coexist (Rankin and Mackay).

Those affected are short because of their short legs, so that the *dwarfism* appears on standing, though it is not noticeable on sitting.

Some of the court fools of former times were achondroplasics. Nowadays many of them earn their living in sideshows or in circuses.

On x-ray examination of long bones like the humerus the diaphysis is found to be broadened at the ends but narrowed in the middle. The epiphyses are plumper than normal.

The disease runs in *families*. Sometimes only *males* are affected through several generations (Porter). As a rule the parents of micromelic children look normal. *Lues* has nothing to do with the disease.

**Diagnosis.**—The condition is easily recognized by the dwarfism, the micromelia, the trident hand, and the enlarged skull. It must be differentiated from *rickets* (intermissions and exacerbations; delayed, instead of premature, ossification; x-ray); (2) from *thyro-aplasia* and *athyreosis* (myxedema symptoms; delayed ossification; benefit from thyroid therapy); (3) from *osteogenesis imperfecta* (x-ray plate; multiple fractures; short duration of life).

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### (*e*) *Osteopsathyrosis and Osteogenesis imperfecta*

In **osteopsathyrosis**, or *Lobstein's disease*, the bones are abnormally brittle. Though the general health of the patient may be good, *fractures* of the bones follow trifling injuries. Thus a man has been known to fracture his jaw while simply chewing. Some patients have undergone

more than 100 fractures. The fractures heal readily, and are often accompanied by pain. Cases have been reported in which this condition was associated with muscular atrophy and polyuria (B. Sachs), but as a rule the disease is unaccompanied by other signs.

The term **osteogenesis imperfecta** has been applied to a disease of the fetus in which the bones fail to develop normally, and at birth and

Fig. 501.—Röntgenogram of the Lower Extremities of a Child Showing Marked Changes in the Epiphyses and Multiple Fractures Marked by ×'s. (X-ray Dept. J. H. H.)

afterwards all the bones are exceedingly fragile. The *calcium-balance* is minus. X-ray examination soon after birth may reveal large calluses due to intra-uterine fractures that have united.

The bones of the skull are defective and the extremities are deformed. Death usually occurs soon, though some patients survive, and the bones may grow firmer later. An interesting case has been studied recently by my colleague, Dr. John Howland, in the Harriet Lane Home.

Metabolic studies in osteogenesis imperfecta have been undertaken by Bookman and by Schabad. The former found that there was deficient calcium-retention in the florid stage. Schabad, who studied a seven-year-old child with osteogenesis imperfecta, found that calcium-retention was deficient. This could be improved by the administration of phosphorus and cod-liver oil. He also described a hyperphosphaturia in association with osteogenesis imperfecta, though there was, as normally, more phosphate in the urine than in the stool.

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## (*f*) *Osteomalacia*

(*Mollities ossium; Spondylolisthesis*)

**Occurrence.**—This form of softening of the bones resembles rickets in many ways, and there has been much dispute as to whether the two diseases are related to one another or are to be kept sharply separated from one another. Women in the reproductive age are most often affected, usually after they have borne children (*puerperal osteomalacia*).

**Symptoms.**—The disease sets in, as a rule, with severe *pains* in the back, hips or extremities; the pains are more marked on movement. The patients fatigue easily, especially on attempting to walk. The *bones* soften and, under the body-weight, they undergo distortion. Deformations of the pelvis, due to healed osteomalacia, may interfere later with childbirth (see Textbooks on Obstetrics). The pelvic inlet assumes a trefoil shape, or that

of the ace of hearts. As the spine softens, marked kyphosis or kyphoscoliosis may develop, and the whole spine becomes shortened. In the severer cases the lower margins of the ribs may come to occupy a lower plane than the iliac crests. The ribs, sternum and clavicles may undergo deformation. The bones of the skull and the extremities, though sometimes deformed, are less often involved. The terminal phalanges of the fingers may become flattened through efforts at support on rising from the sitting position.

An early sign is *difficulty in walking,* dependent partly upon pain, but still more upon enfeeblement of the muscles (*osteomalacic paresis*). Adductor spasm of the thighs is a common accompaniment.

Nervous and mental symptoms may coëxist (feeble memory, apathy, indecision, irritability, occasionally dementia).

The disease may last a long time, with many remissions and exacerbations, especially after pregnancies. In fatal cases there is often a terminal infection (bronchopneumonia, sepsis). The patients may be long bedridden. Many suffer from myocardial insufficiency, secondary to the thoracic deformation.

The disease is, fortunately, rare. It seems to be especially prevalent in certain areas (endemic) and to be absent from others. At autopsy the bones may be soft and flexible; sometimes one can cut through the bone with a knife without causing grating. Histologically there are signs of osteoclastic absorption, followed by formation of uncalcified osteoid tissue.

**Pathogenesis.**—Some think the disease related to disturbances of function of the thyroid gland or of the ovary (increased function). Sellheim (1913) believes that the gonads build an internal secretion that exerts an inhibitory influence on bone-growth, and that the secretion is periodical, synchronous with the periodicity of the reproductive life. Chemical studies of the bones show great diminution of all the mineral constituents. According to McCrudden, along with the decrease in calcium there is an increase of magnesium and sulphur, due to the newly-formed uncalcified osteoid tissue. Metabolic studies during the disease show a negative calcium-balance (Goldthwait). The phosphoric acid of the feces is increased (Zuntz). According to the Italian school, osteomalacia is an infectious disease (diplococcus). Cases of osteomalacia in males (virile osteomalacia) have been described; here the pelvis does not seem to be affected, but rather the spine and the extremities.

In women, double oophorectomy may or may not be followed by improvement or recovery, though the calcium-loss temporarily gives place to calcium-retention after the operation. But, in females, osteomalacia can occur independently of pregnancy and of the puerperal period (*juvenile* and *senile forms*).

One type of osteomalacia is met with in early childhood (Rehn). This *infantile osteomalacia* has been separated from rickets, but the identity of

the two diseases is maintained by some. It may be that the two diseases are different expressions of one and the same process (Vogt).

**Diagnosis.**—This is easily made in the well-developed cases. Recognition is often extremely difficult at onset, when the disease may be mistaken either for rheumatism or for sciatica. Röntgenograms and adductor spasm are helpful in differentiation.

Multiple myeloma of bones may give rise to similar symptoms, but, in Kahler's syndrome, the bones are not flexible, and the patients can walk, at least until near the end. The Bence-Jones protein may occur in the urine in both diseases. The remarkably beneficial effect asserted to have followed removal of the ovaries in some cases of severe osteomalacia is worthy of notice.

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## (g) *The Bamberger-Marie Disease*

*(Hypertrophic Pulmonary Osteo-arthropathy, Toxicogenic Osteoperiostitis ossificans of Sternberg)*

**Definition.**—A disease affecting the skeleton symmetrically, characterized by clubbing of the ends of the fingers and toes, and by enlargement of the distal extremities of the long bones near the joints.

**Symptoms.**—The sites of predilection for the enlargements are the distal extremities of the ulna and radius and of the tibia and fibula. The

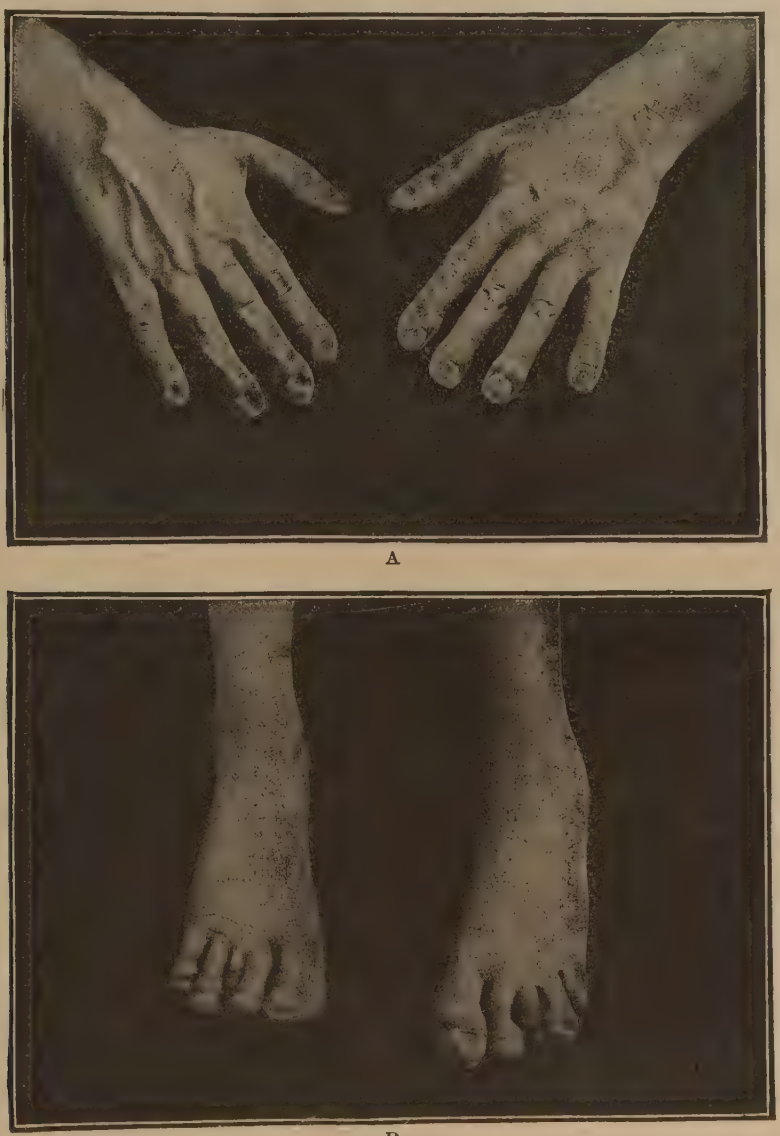

Fig. 502.—Clubbed Fingers and Toes in a Case of Congenital Cyanosis. (After Quisez, Arch. d. mal. d. cœur, published by Baillière et Fils, Paris.)

joints themselves are free, so that the term "osteo-arthropathy" is a misnomer. The bones of the hands are less affected than those of the forearm and leg. In the spine there may be kyphosis or scoliosis.

The thickening of the bones is due to a slowly ossifying periostitis and osteitis of variable grade.

The soft parts are also thickened over the enlarged bones; this is most striking at the finger-tips. The finger-nails may be markedly curved so as to assume a watch-glass form. Even markedly clubbed finger-tips (hippocratic fingers; drum-stick fingers) may, in röntgenograms, show but little if any bony change.

Occasionally the ribs, the sternum, the clavicles and the pelvic bones are involved. When the metacarpal bones of the hands are affected an x-ray plate reveals distinctly the periostitis along the shaft.

**Pathogenesis.**—The condition is secondary to various primary diseases, especially to chronic suppuration (lungs, bladder, renal pelvis). The commonest associated conditions found in the lungs in Marie's disease are (1) tuberculosis, (2) bronchiectasis, (3) empyema and (4) neoplasm. The condition has also been met with in congenital heart disease, in dysentery, in lues and in various infectious processes.

Clubbing of the fingers can occur independently of toxicogenic osteoperiostitis, though Sternberg is probably right in regarding the change in the fingers as an initial phenomenon of the skeletal disease, which, sometimes, does not develop fully.

**Diagnosis.**—The disease is easy to recognize. It will scarcely be confused with acromegaly, in which the whole hand is enlarged, and in which the characteristic changes in the skull occur; moreover, x-ray plates show the diaphyseal periostitic thickening characteristic of Marie's disease.

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### (*h*) *Acromegaly, Gigantism, Dwarfism, Infantilism*

These conditions, in which the growth of bone is either increased or diminished, and the epiphyses unite either too late or too early, are described under Diseases of the Endocrine Glands (see Part XIV).

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### (*i*) *Leontiasis ossium*

(*Megalocephaly; Hyperostosis cranii*)

In this condition there is hyperostosis of the bones of the skull, involving chiefly the cranial skull, though sometimes the facial skull is also enlarged. Cases have been studied in this country by M. Allen Starr of New York, and by J. J. Putnam of Boston. In Starr's case, there was a slowly progressive growth of the head, face and neck, involving both the bones and the soft tissues over them—a true *megalocephaly*. According to Putnam, osteophytic growths from the inner table of the skull may cause symptoms like those of brain tumor.

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### (j) *Oxycephaly; Pyrgocephaly*

*(Tower Skull or Steeple Head; Turmschädel)*

In certain persons the upper part of the head attains to an unusual height, giving rise to a high forehead, which slopes to a *pointed vertex* like a tower or steeple. The supra-orbital ridges are low. The hairy scalp begins at a high level. The patients suffer from *headache* and from *impairment of vision,* due to gradually developing *optic atrophy.* In many of the patients, there is *exophthalmos* and *anosmia.*

Fig. 503. — Oxycephaly. Case in the Basler Kinderspital. (After R. Bing.)

The disease appears to be associated with *premature synostosis of the sutura coronalis and the sutura sagitallis.* This restricts the growth of the vault of the skull in the anteroposterior and in the transverse diameter; to provide for the increasing bulk of the brain, there is a compensatory increase in the height of the skull. The *fonticulus frontalis* closes late and its former site may project a little. The optic atrophy is secondary to choked disk from increased intracranial pressure, just as in tumor of the brain. It would be interesting to know whether or not an early decompression-operation, as Osler recommends, would be helpful in such cases.

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## 3. The Osteopathies of Circulatory Origin

Under this heading we shall include, (a) gangrene of the foot and toes, and (b) Barlow's disease.

### (a) *Gangrene of the Foot and Toes*

**Definition.**—Death of the distal portion of the lower extremity as a result of anemia dependent upon occlusion of the artery supplying the part.

**Etiology.**—In old people the condition is due to *arteriosclerosis* with thickening or thrombosis (senile gangrene). In younger people, it is also due to arterial occlusion, either from *syphilitic arteritis,* from arteriosclerosis developing in *diabetes,* or from thrombosis in *acute infections* (typhoid, *thromboangeitis obliterans*).

**Symptoms.**—The patients begin to notice *pain* or *paresthesia* in the toes and foot. Sometimes *intermittent claudication* (*q. v.*) precedes the

symptoms of gangrene. The patients may have noticed that the foot grows *pale* at times, or that it is unusually *livid* at other times.

On physical examination the signs of *arterial change* may be found. The blood pressure need not be elevated. Palpation of the A. dorsalis

Fig. 504.—Röntgenogram of the Upper Extremity Showing Superiosteal Hemorrhage in Infantile Scurvy—Barlow's Disease. (X-ray Dept. J. H. H.)

pedis on the medial margin of the dorsum of the foot and of the A. tibialis posterior below the medial malleolus, may reveal *absence of pulsation* or a very feeble pulse.

In the differential diagnosis, *Raynaud's disease, acrocyanosis anesthetica,* and *erythromelalgia* should be considered.

### (*b*) *Barlow's Disease*

This condition, known also as *infantile scurvy,* has already been described (see Part VII).

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## 4. The Inflammatory Osteopathies

The inflammation may involve the bone itself (*osteitis*), the bone-marrow (*osteomyelitis*), or the periosteum (*periostitis*). In addition, cavities lined by mucous membrane within the bones may be the seat of severe inflammation; thus we have already described *paranasal sinusitis* in the maxillary, frontal, and other sinuses (see Part V); similarly, the middle ear or the internal ear may be the seat of inflammation (*otitis media, otitis interna*).

Fig. 505.—Röntgenogram of the Leg in Osteomyelitis. The Arrows Point to Cavities Filled with Iodoform Packs. (X-ray Dept., J. H. H.)

Inflammations of the bone may be due to ordinary *pyogenic microörganisms* (streptococci, staphylococci, etc.), or to the *typhoid bacillus*, as in typhoid periostitis. But we see also many instances of so-called *specific* inflammations (*tuberculosis, syphilis, actinomycosis* and *sporotrichosis*), due respectively to the *Bacillus tuberculosis*, the *Treponema pallidum*, the *Actinomyces* fungus, and the *Sporotrichum* fungus.

### (*a*) *Acute Osteomyelitis*

**Definition.**—An acute infection of the bone-marrow, usually involving bones in different parts of the body, though sometimes limited to a single bone, and dependent upon hematogenous infection, most often with the *Staphylococcus pyogenes aureus*, sometimes with the *Streptococcus* or other pathogenic bacteria.

**Symptoms.**—The disease is more common in young children and in adolescence than in adults. The *portal of entry* of the staphylococcus may be obvious or it may be obscure. The patients sicken with *chills, high fever*, and *tachycardia*, and they often manifest *delirium*.

The *course* of the disease is usually rapid. Many patients die before a diagnosis is made, and the true nature of the condition is discovered only at autopsy. If the condition be suspected, and *local pain* be complained of, palpation of the bone, if it be accessible, may reveal *local swelling* and *tenderness*. Common *sites* are the shaft of the femur, the clavicle, scapula, a rib, and the tibia. Any bone may, however, be involved, including the bones of the skull, the spine, the clavicle, the sternum, and the small bones of the extremities. If the patient live long enough and the disease be acute, *abscesses* usually form in and around the affected

bone. Often a considerable mass of bone dies (*necrosis of bone*), and the *sequestrum* will keep up chronic suppuration, with sinus formation, unless an operation be performed.

**Diagnosis.**—The symptoms and signs may be distinctive, especially if opportunity for infection be known. When the condition is suspected, a *blood culture* should be made, and will often reveal the bacterial cause. It is important to remember that in osteomyelitis during adolescence the urine may contain the etiological agent. I once grew the staphylococcus in *cultures from urine* drawn aseptically from the bladder in a young physician suffering from osteomyelitis.

In the **differential diagnosis,** we must distinguish acute osteomyelitis (1) from *acute arthritis,* especially from *acute coxitis;* (2) from *subcutaneous* and from *intramuscular abscess;* (3) from *acute rheumatic fever;* (4) from *ordinary septicemia* and *pyemia;* and (5) from *malarial fever.*

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## (*b*) *Chronic Ostitis and Osteomyelitis*

This is often confused with *syphilis,* with *tuberculosis,* with *actinomycosis,* with *sporotrichosis,* and with *sarcoma* of bone (see Examination of the Tibial Region). The anamnesis and a thorough physical examination, together with röntgenograms, and serodiagnostic tests, will differentiate these processes. In case of operation, *cultural methods, animal inoculations,* and *histological studies* will remove all doubt as to the nature of the process.

A special form of chronic ostitis, known as ostitis fibrosa (or v. Recklinghausen's bone disease) is occasionally met with.

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### 2. *Ostitis fibrosa (v. Recklinghausen)*

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### (c) *Acute Periostitis*

**Definition.**—An acute inflammation of the covering of bone (periosteum).

**Etiology.**—Acute periostitis follows either *trauma,* as in fracture or contusion, or *infection,* as in acute periostitis of the jaw secondary to dental infection. An acute periostitis is not uncommon as a complication of *typhoid* fever, and may be due either to the typhoid bacillus itself, or to complicating secondary infections.

**Symptoms.**—There is local swelling, extreme pain, and heat. In the septic cases, suppuration may follow. In the purely traumatic cases, the condition is usually transitory.

**Diagnosis.**—This is usually easy if the etiology be known. X-ray examinations will differentiate acute from chronic periostitis, since in the latter there will be evidence of bone-formation. The syphilitic forms of periostitis are described below.

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### (*d*) *Chronic Periostitis*

Any acute periostitis may become chronic or a periostitis may be chronic from the beginning, as in syphilis (see Syphilis of the Bones), or in the pathogenic osteoperiostitis of Sternberg (see Marie's Disease).

### (*e*) *Syphilis of the Bones*

(*Syphilitic Osteitis and Periostitis; Luetic Bone Affections*)

**Occurrence.**—The bones may be affected either in hereditary or in acquired lues. In the latter, the bones may be involved either in the secondary or in the tertiary stage of the disease.

#### i. The Bones in Secondary Lues

The patients often complain of "rheumatic" or of "neuralgic" pains, or of circumscribed tenderness on the bones. The superficial bones (skull, anterior surface of tibia, ulna, metacarpi) are most often affected. The pains are milder in the daytime than at night when they may become almost insupportable (*dolores osteocopi*). Nodes, due to subperiosteal deposits, often become palpable.

#### ii. The Bones in Tertiary Lues

Here gummata appear, either in the form of a circumscribed periostitis, causing round *nodes,* sensitive at first, and, later, more indolent. Sometimes these nodes soften and break down; occasionally there is fistula-formation. Gummata beginning in the marrow and in the spongy part of long bones are less common. They sometimes occur, however, in the phalanges, in the radius, or in the ulna. When a phalanx (dactylitis syphilitica), or a metacarpal bone, is affected, the appearance may resemble that of a tuberculous "spina ventosa."

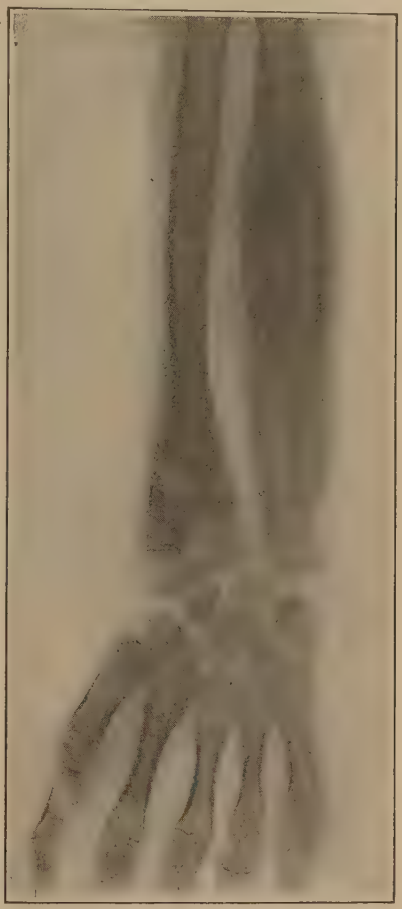

Fig. 506.—Röntgenogram of the Forearm and Hand Showing Syphilitic Osteitis and Periostitis. (X-ray Dept. J. H. H.)

In x-ray pictures the signs of syphilis of the bone are usually characteristic. Thus, in simple luetic periostitis, a lamellation of the periosteum

may be visible, running parallel to the cortical wall of the bone. Sometimes a circular involvement of the bone is recognizable.

In gummata of bone the involvement may be devoid of structure in the x-ray plate; the bone is always more transparent in the area affected. In the periphery the bony shadow may be more intense in places (*osteoscle-*

Fig. 507.—Röntgenogram of the Hand of a Child with Congenital Lues, Showing Periostitis. (X-ray Dept. J. H. H.)

*rosis*), and less intense, or spotted, in others (*osteoporosis*). Nodes and spindle-shaped swellings are often easily visible in röntgenograms.

The mouse-eaten, or mosslike, appearance of the periosteum in some cases of luetic periostitis is very characteristic.

**Diagnosis.**—Lues of the bones may be mistaken for *tuberculosis,* for *sarcoma,* for *sporotrichosis,* or for *chronic staphylomycotic osteomyelitis,* but the clinical history, the nocturnal pains, the sites of predilection, the x-ray plates, and the positive Wassermann reaction make the diagnosis easy.

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## (*f*) *Tuberculosis, Actinomycosis and Sporotrichosis of the Bones*

These important subjects, though they belong chiefly to surgery, have been already referred to (see Part XI, Methods of Examination, and also Part IV, Infectious Diseases).

Fig. 508.—Röntgenogram of Spine; Tuberculosis of 10th, 11th, and 12th Thoracic Vertebrae. The Arrows Point to Areas of Destruction. (X-ray Dept., J. H. H.)

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## (g) Paget's Disease

*(Osteitis deformans; Senile Pseudorickets)*

**Definition.**—A disease, described by Paget in 1876, which begins usually after middle life, progresses very slowly, and is characterized by pains in the bones and by marked deformations (particularly enlargement of the skull and of the clavicles, cervicothoracic kyphosis, enlargement of the lower aperture of the thorax, and a bowing of the lower extremities forward and lateralward); the bony tissues soften (owing to rarefying osteitis), and thicken (owing to subperiosteal and medullary new-bone formation), and the bones become abnormally curved.

**Etiology.**—The cause is unknown. The malady is often a family disease. Through the courtesy of Dr. Marie Ingram, of Baltimore, I have had the opportunity of observing and of exhibiting at my clinic one of these interesting families. Paget's disease should be sharply separated from the similar lesions produced by syphilis, with which it has nothing to do. An association with atherosclerosis is very common. In a group of cases very carefully studied by Locke, of Boston, atherosclerosis was a marked feature.

**Symptoms.**—As a rule, the symptoms develop after the fiftieth year, with pains and with enlargement of the bones.

The *onset* of Paget's disease is insidious, the deformations often being quite marked before they are accidentally noticed. In other cases rheumatic or neuralgic pains may precede the deformity by years or by decades. One bone after another may become affected—in order of frequency: the skull, the tibia, the femur, the pelvic bones, the spine, the

clavicles, the ribs, and the radius. The disease may or may not be bilaterally symmetrical.

The bones of the legs are usually affected early, but the patients continue to walk, in spite of marked deformity, and, indeed, the contrast between the severity of the anatomical disturbance and the degree of preservation of function is characteristic. The deformity seems to be due

Fig. 509.—Paget's Disease or Osteitis Deformans. (Med. Service J. H. H.)

Fig. 510.—Osteitis deformans, Paget's Disease. Showing the Simian Attitude, the Large Head, the Flaring Ribs, Transverse Abdominal Sulcus, and Marked Bowing of Both Femora and Tibiae. (After S. H. Hurwitz, J. H. H. Bull.)

mainly to the softening and to a pathological growth of bone in the longitudinal direction on the convex side. Through the curving of the long bones the body height may be markedly diminished. Osler mentions a patient in whom the reduction in stature was no less than thirteen inches. When the ribs and sternum are much deformed respiration is impeded; it may become wholly diaphragmatic. These changes in the bony thorax may

account, in part, for the bronchitis and for the myocardial insufficiency that are common complications. The enlargement of the skull may be very great; the circumference may reach 60 or even 70 cm.

The bones affected may reach a size twice as large as the normal bones. On palpation one makes out immediately that the enlargement is due to bone and not to the soft parts.

The changes in the *skull* may resemble those seen in hydrocephalus, the whole head assuming the form of a triangle, with the base upward. The projecting frontal bones give the impression of an "Olympic" forehead, and the parietal bones remind one, to a certain extent, of a rachitic skull; but there are no abnormal depressions, the bulgings are even, the sutures are not sunken, and the fontanelles are completely closed.

The *face* is relatively small, and is usually obliquely placed. The bones of the face may participate in the hypertrophy; thus, the zygomata may become thickened, and healthy teeth may be squeezed out of the jaw owing to thickening of the jaw-bone encroaching upon the cavities holding the teeth (Marie and Léri). The spine is often kyphotic, but usually not scoliotic. The *ribs* are broad and thick and the costal cartilages become ossified. There is often lateral flattening of the thorax. The *pelvis* is broad and the crests of the ilia become thickened. The *clavicles* are markedly thickened and excessively curved; they may hang down as "garlands" over the thorax. The *radius* may be markedly changed, but the other bones of the upper extremities are usually but little affected. Röntgenograms of the hands and feet may reveal great enlargement of single *metacarpal bones.*

The **external appearance** of the Paget patient is very characteristic. On walking, the cervicothoracic kyphotic curvature of the spine, with the head inclined forward, is a striking feature. The skull looks unusually large in comparison with the relatively small face. The abdomen is prominent, and is separated from the cylindrical thorax by a deep transverse depression. The violin-shaped body is supported by lower extremities, which, though shortened, are large around. The patient walks with a broad base and with caution, lest one foot stumble over the other. The upper extremities look relatively too long, the finger-tips often reaching almost to the knee, owing to the shortening due to the curvatures of the spine and of the legs. In typical cases the apelike appearance of the patient is striking.

The *calcified arteries* are a marked feature in x-ray pictures of the extremities. Cardiovascular changes are so common that some clinicians make them a part of the symptom-complex of Paget's disease (Dieulafoy). Occasionally, a patient becomes bedridden, but this is rare. Those affected live for decades, suffering much from pains, from atherosclerotic disorders or from chronic bronchitis. As the disease advances, the pains fortunately grow less. Gout and carcinoma are not uncommon in the end stages.

**Diagnosis.**—Röntgenograms are very helpful in deciding upon the nature of the disease. The bony structure presents a strange cotton-wool-like appearance in both the diaphysis and the epiphysis. The cortical zone of the bone is more transparent than normal, owing to thinning of the subperiosteal layer. The base of the skull shows peculiar changes, for which A. Léri has set up an especial röntgenographic formula.

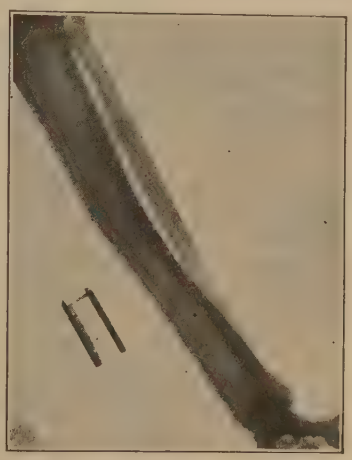

Fig. 511.—Osteitis deformans. Röntgenogram of Tibia and Fibula: Tibia Irregularly Thickened with Longitudinal Areas of Porosis; Fibula Shows Little Calcification, but Longitudinal Areas of Porosis. Marked Sclerosis of Posterior Tibial Vessels. (After S. H. Hurwitz, J. H. H. Bull.)

Paget's disease must be differentiated (1) from *acromegaly* (the facial rather than the cranial skull is hypertrophic; the acra (hands and feet) are enlarged; big sella turcica in x-ray plate); (2) from *leontiasis ossea* (head alone involved); (3) from *chronic arthropathies* (diaphyses of long bones unaffected; röntgenograms); (4) from *rickets* (age, rickety rosary, depressed fontanelles, x-ray); (5) from *osteomalacia* (softening of bones without hypertrophy, x-ray); (6) from *syphilitic osteitis*, especially from that affecting the tibia in hereditary syphilis (x-ray, Wassermann reaction); (7) from *senile osteoporosis*, or *pseudo-Paget's disease*, in which there is kyphosis of the thoracic spine and bow-legs, but no hypertrophy of the bones and no deformation of the skull, of the clavicles or of the upper extremities.

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## 5. The Neuropathic Osteopathies

In *syringomyelia* and in *tabes* disturbances of bone are not uncommon. Spontaneous fracture may occur from increased fragility. In the *Morvan type* of syringomyelia, there may be gradual disintegration of a finger-tip similar to that which occurs in *leprosy* and in *Raynaud's disease.*

A perforating ulcer of the foot (*malum perforans*), so common in tabes, while it involves, at first, only the soft parts, may, later on, cause destruction of the underlying bone.

## 6. The Parasitic Osteopathies

The bones are tolerably immune from invasion by animal parasites, largely owing to inaccessibility.

Flexner, however, has described a necrosis of the jaw-bone in which amebae were present, probably the *Entameba buccalis,* which we now know to be so frequently associated with pyorrhea alveolaris.

*Echinococcus cyst* may also be located within bone.

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## 7. The Neoplastic Osteopathies

These include *benign tumors* like osteomata and chondromata, and the *malignant tumors,* sarcoma and metastatic carcinoma.

The so-called *cholesteatoma* is not a true tumor, but the product of the chronic desquamative inflammation so common after destructive otitis media in scarlet

fever. *Cartilaginous exostoses* are probably to be regarded not as true tumors, but as congenital osteopathies (*q. v.*).

*Osteomata* are easily recognizable by their ivory hardness. *Chondromata* or *enchondromata* form firm, nodular, usually rounded masses, which may attain to very large size. They are not so hard as osteomata.

*Sarcoma* of bone often takes the form of **myeloid sarcoma,** containing giant cells. Other sarcomata may arise from the periosteum, in which event there is no bony covering to the tumor on its surface.

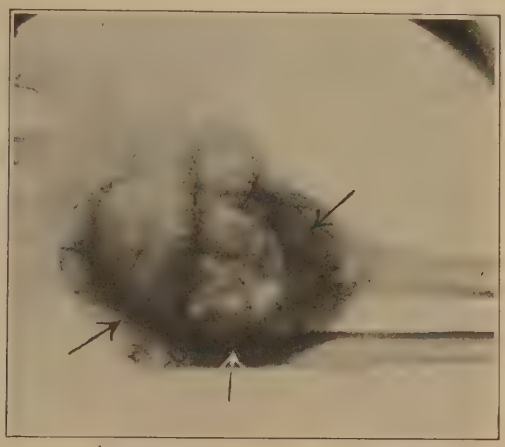

Fig. 512.—Röntgenogram of Wrist Showing Giant-Celled or Myeloid Sarcoma. (X-ray Dept. J. H. H.)

On the gum, the so-called **epulis** may be either a pure fibroma, an ordinary sarcoma, or a giant-celled sarcoma. When the mass has the color of the normal gum and is firm, it is probably a pure fibroma; when of the same color, but softer, it is probably a sarcoma; if of a darker color and somewhat brownish, it is a giant-celled sarcoma. Some reserve the name epulis for this giant-celled form. An epulis may return locally after removal, but it does not form metastases, nor are the regional lymph glands involved. Chronic irritation predisposes to the development of epulis. We see epulis appear not infrequently in the lacunae formerly occupied by a tooth, or in the neighborhood of the stump of a tooth.

A *clavicle* is sometimes the site of a sarcoma. When one clavicle is enlarged, a primary sarcoma should be suspected, especially if a metastatic carcinoma from the thyroid, breast, or prostate, can be ruled out. Tuberculosis or gumma of the clavicle may simulate sarcoma, and Paget's disease sometimes attacks a single bone, causing diffuse enlargement.

One of the most interesting forms of sarcoma is the myeloid sarcoma that attacks the *upper end of the tibia* and sometimes the *lower end of the radius.* Some of these tumors form a radish- or turnip-like enlargement of one end of the bone, and parchment crackling can be felt over it. On auscultation, a bruit may be audible, owing to the vascularity of the neoplasm. These sarcomata are often spoken of as **bone cysts** or **bone aneurisms,** on account of the blood they contain. The x-ray picture is very characteristic, and the size of the mass rules out abscess. This form of sarcoma not infrequently affects the shafts of the long bones, and every spindle-shaped enlargement of a shaft should be regarded as suspicious.

In a certain number of cases these masses are not true tumors, but a form of inflammation (osteitis fibrosa); others occur as the result of trauma (anomalous callus). In the femur a sarcoma of the shaft, with blood cyst formation, may be the cause of spontaneous fracture.

**Metastatic carcinoma** is common in the bones of the skull and in the bones of the pelvis, but causes most symptoms when it attacks the bones of the spine and compresses the roots of the spinal nerves, with characteristic root pains (very common in the metastases from carcinoma of the breast, thyroid and prostate). These metastases, when suspected, can usually be easily demonstrated in röntgenograms.

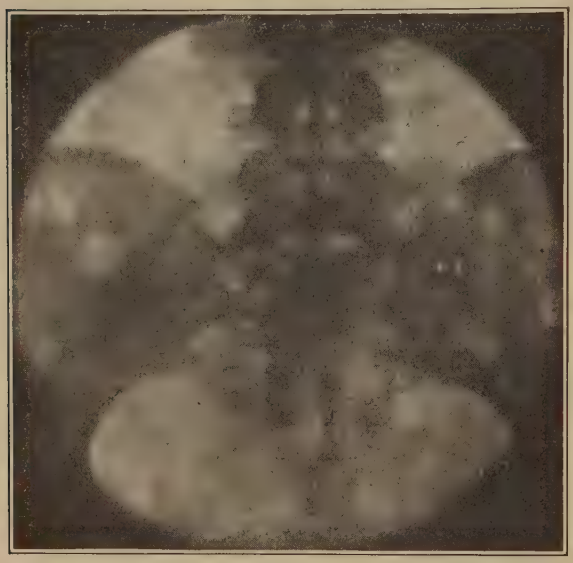

Fig. 513.—Carcinomatous Metastases in Both Ilia in a Case of Carcinoma of the Breast Showing Bence-Jones Proteinuria. (After T. R. Boggs & C. G. Guthrie, J. H. H. Bull.)

**Multiple myeloma** of bone or *Kahler's syndrome* is a disease characterized clinically by (1) deformations of the bones of the trunk due to the tumors; (2) severe, intermittent pains in the affected bones, and (3) the presence of Bence-Jones body (*q. v.*) in the urine. (See Part VII.)

The disease must be differentiated from other multiple tumors of bone (primary or secondary). Among these, carcinoma metastases, sarcomata, endotheliomata and hypernephromata should be considered. In the metastatic tumors, the spine, the pelvic bones, the femur, the ribs, the sternum, the humerus, and the flat bones of the skull are most often involved.

Bone tumors usually show well in *röntgenograms,* and, if the tumors involve the marrow, *myelocytes* will, as a rule, appear in the blood, an important diagnostic sign.

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# C. Special Diagnosis of Diseases of the Joints

The principal diseases of the joints may be conveniently subdivided into:

I. The congenital arthropathies.
II. The static and the toxic degenerative arthropathies.
III. Arthropathies of circulatory origin.
IV. The inflammatory arthropathies (the arthritides).
V. The neuropathic arthropathies.

## 1. The Congenital Arthropathies

Under this heading are included, *absence of joints, congenital dislocations* of joints, and the *congenital forms of club-foot,* and *flat-foot.* These properly belong to surgery rather than to medicine. The internist should pay especial attention to the recognition of *congenital dislocation of the hip.* The main features have already been described under Methods of Examination.

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## 2. The Static and the Toxic Degenerative Arthropathies

It must be kept in mind that an extremity is a *static unit* and that disturbance in one part of this unit will secondarily affect other parts; for example, a flat-foot or a genu vâlgum will influence the hip joint, and pathological alterations in the hip joint will, in turn, influence secondarily the knee and ankle joints. Secondary disturbances of this sort are known as static disturbances of the joints. Preiser, in a large monograph, on **static arthropathies,** asserts that much of the so-called arthritis deformans or hypertrophic osteo-arthritis is to be looked upon as static in origin.

It seems likely that the **villous arthritis** of Goldthwait, especially common in the kneejoint, has also a static origin, as it occurs often in obese persons, on whose joints unusual strain is thrown. The origin of flat-foot from over-weight may also be regarded as a static disturbance.

Of *toxic degenerative* disturbances in the joints, we have but little definite information. Some believe that certain forms of chronic arthritis are to be regarded as toxic degenerative conditions rather than as distinct inflammations. Thus, it has been asserted that hypertrophic osteo-arthritis is toxic in origin, and others think that even some forms of exudative arthritis have a toxic origin.

In this connection, two interesting changes met with about the joints may be referred to; though easily recognized, the beginner may be puzzled by them. I refer to (1) ganglion carpi, and (2) lipoma arborescens.

**Ganglion carpi.**—In ganglion carpi, a spherical or villous mass appears on the dorsum of the carpus. The mass is due to a gelatinous degeneration of the connective tissue of the capsule of the wrist joint. It is not connected with the synovial membrane, either of the joints or of the tendons, though formerly tendogenous and arthrogenous ganglia were described and presumably differentiated from one another. The patient is surprised at the sudden disappearance of a ganglion when it is given a sharp blow with the flat side of a book.

**Lipoma arborescens.**—In obese women, about middle life, it is very common to find below either the medial malleolus or the lateral malleolus, a lobulated, flat, tumorlike mass. This is the well-known lipoma arborescens. It is very common in connection with different forms of chronic arthritis or of chronic irritation of the joints.

It depends upon fatty degeneration of a part of the synovial membrane of the joint.

Lipoma arborescens is common also in the knee-joint, where the villi especially at the upper recess of the synovial sac, may undergo fatty degeneration. In the case of the knee, this lipoma arborescens may not be discovered until the knee-joint has been opened surgically.

**Relaxation of Sacro-iliac Joint.**—In many instances pain in the back or down one thigh is due to relaxation of the sacro-iliac articulation. To test for this, the leg of the patient is fully extended at the knee; we place one hand over the patella and with the other lift the heel. If there be relaxation of the sacro-iliac joint, or arthritis of this joint, the patient will then usually feel pain down the back of his thigh, for the ham-string muscles are attached to the ischium and the movement described tends to displace the ilium on the sacrum and to cause pressure on the lumbo-sacral cord (Goldthwait).

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## 3. Arthropathies of Circulatory Origin

Under this heading brief mention must be made of hemarthros.

### (*a*) *Bleeder's Joint*

*(Hemarthros; The Hemophilic Joint)*

**Etiology.**—Hemorrhage into a joint, aside from that due to severe trauma, occurs in patients who are victims of a hemorrhagic diathesis (hemophilia, purpura, scorbutus, etc.). This diathesis is congenital in hemophilics, but acquired in purpura, scurvy, etc.

**Symptoms.**—The condition is commonest in one or both of the knee-joints. The signs of a chronic joint effusion develop.

**Diagnosis.**—The anamnesis may give the clue to the existence of a hemorrhagic diathesis. The appearances in röntgenograms are characteristic. The condition may be mistaken for other forms of chronic arthritis (chronic infectious arthritis, tuberculous arthritis, or lues).

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# 4. The Inflammatory Arthropathies (the Arthritides)

## (a) *Classifications of Arthritis*

Writing on this subject in 1913 I said:

"In no part of medicine, perhaps, have *names* been used less satisfactorily than in designating the arthropathies; we find, on the one hand, one malady masquerading under many different names, or, on the other hand, one name used ambiguously, meaning sometimes one disease, sometimes another, or sometimes a group of separable diseases. Even today there are scarcely two authors in one country who use precisely the same terminology for the arthropathies; add to this the varying use of terms by writers of different nationalities and the lack of uniformity of expression becomes very perplexing. Notwithstanding, however, all the confusion that exists regarding names, a study of their history will reveal the fact that the introduction of each corresponded to some special conception, and that, for the purpose for which it was chosen, it usually served a useful function. The difficulties that have arisen have been largely due to the attempts made to force classification and names made for different purposes into coincidence with one another. Ignoring the original purpose of a name, writers not infrequently use it for a wholly different purpose, with subsequent disorder and excitation of controversy. A comparison of the cases of joint disease with which one is familiar in America with the cases described by writers in Great Britain, Germany, Austria, and France makes it clear that the material in different countries is not dissimilar."

Fully to understand the way in which the various terms used in describing arthritis have undergone modification, a certain familiarity with the *history of the subject* is helpful, and for this the reader may consult my report at the International Medical Congress in London in August, 1913. I have made liberal use of this report in writing the following pages. For an admirable discussion of the *pathogenesis* of the different forms of chronic joint disease the report of Friedrich von Müller made at the same congress should be consulted (see Reference).

The tendency at present is to apply the word **gout** only to processes dependent upon abnormalities of the metabolism of purins, to use the term **arthritis** as a general term for inflammation of a joint, no matter what its cause, and to reserve the term **rheumatism** (if it be kept in use at all) for the group of inflammatory joint diseases due to the virus that is the cause of acute rheumatic fever (true).

A study of the *terminology* that has been used in connection with the arthropathies indicates that the distinctions that the morbid anatomist needs and that suffice for his purposes, may be very different from those necessary for the clinician in his work or for the etiologist in his studies; hence the *purpose* of a given name or a given classification should always be definitely understood.

In all medical work we have to deal with a world of rough distinctions and must ever be on guard against the fallacies that abound wherever distinctions are imperfect.

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## (*b*) *Acute Arthritis*

For a long time, *acute rheumatism* was the name applied to any acute arthropathy not traumatic or gouty in its origin, but gradually the term **acute rheumatic fever,** or *acute articular rheumatism,* has come to be limited to that acute febrile peri-articular affection that often follows tonsillitis, is frequently complicated by endocarditis, pericarditis, or chorea, does not lead to suppuration of the joints, but responds promptly to treatment with salicylates and ends in recovery without residual joint change. This acute rheumatic fever (true) has been, and is still, separated from (1) *the pyemic joint infections,* (2) *gonorrheal arthritis,* and (3) *certain acute polyarthritides* complicating the acute exanthemata, typhoid, dysentery, mumps, syphilis, etc. Some authors have grouped the acute, non-suppurative peri-articular joint diseases that resemble acute rheumatic fever (true), but differ from it in several important particulars (cause, course, occasional suppuration, relative inefficacy of salicylates), together under the name of the **pseudorheumatisms** (Bouchard), or the **rheumatoids** (Gerhardt).

Fig. 514.—Schönlein's Disease. Purpura with Infectious Arthritis. (Med. Service, J. H. H.)

When the bacteria causing a given pseudorheumatism could be determined, a corresponding special name was applied (*e. g., Polyarthritis gonococcica; P. streptococcica; P. staphylococcica*). Some assert that there is no acute rheumatism (true) separable from this series of pseudorheumatisms; others assume (and at present the writer agrees with them) the independence of an acute rheumatic fever (true), a *polyarthritis rheumatica acuta* of specific etiology.

Whether or not the bacteria described by Poynton and Payne, or the peculiar, oxygen-sensitive streptococci described by Rosenow of Chicago, represent this virus further studies must show. Arthur Bloomfield has confirmed Rosenow's findings in a number of the writer's cases.

The diagnosis of acute rheumatic fever (true) is discussed in the section on infectious diseases (see Part IV, Subdivision II).

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[Note.—See also references on Acute Rheumatic Fever, Part IV.]

## (*c*) *Chronic Arthritis*

Here classifications differ according to the purposes of the *morbid anatomist,* the *etiologist,* and the *clinician,* respectively.

### i. Pathological Anatomical Grouping

A. Chronic arthropathies classified according to the site of the lesion.

1. Involvement of the whole joint (*e. g., panarthritis*).
2. Involvement of the soft parts about a joint (*e. g., periarthritis, periarticulitis, arthromeningitis externa*).
3. Involvement especially of the synovial membrane and its villi (*e. g., synovitis* [or *arthromeningitis*] *interna, arthritis, villosa*).
4. Involvement especially of the cartilages and bones of the joint (*e. g., arthritis deformans, osteo-arthritis deformans*).

B. Chronic arthritis classified according to the kind of morbid anatomical process concerned (nature of the lesion).

1. The toxic degenerative or metabolic inflammations in the joints (*e. g.,* the *gouty arthropathies*).

2. Chronic *alterative* inflammations of the joint, in which retrogressive changes predominate, though with them are associated less exudative and productive processes (*e. g.*, the *atrophic arthritis* of Goldthwait, and of Nathan).
3. The chronic *exudative* inflammations (including *chronic gonorrheal arthritis, tuberculous arthritis,* various forms of *chronic infectious arthritis,* in which, in the early stages, there is effusion or periarticular swelling).
4. The chronic *productive* inflammations in which proliferative changes in the fibrous tissues, cartilage or bone predominate. Such an arthritis may be: (a) the end stage of an acute or subacute arthritis, or of an exudative arthritis of insidious onset, slowly progressing; (b) an arthritis that has been dry and productive from the beginning—the *arthrite sèche* of French writers; or (c) the so-called specific inflammations or infectious granulomatoses.

Such a chronic productive arthritis may affect chiefly the *joint capsule,* or the *bones and cartilages.* In the former instance, the clinical picture is that of the *primary chronic progressive polyarthritis* of His and Hoffa. If there be fibrosis and shrinking of the capsule with adhesion of the joint surfaces, the arthritis is spoken of as a *chronic adhesive* or *chronic ankylopoietic arthritis* (Ziegler), often leading to fibrous, or to osseous, *ankylosis.* In the spine, the ankylosing spondylitis gives rise to the so-called *poker spine.*

When the productive inflammation affects chiefly the bones and cartilages, a so-called deforming arthritis (*arthritis deformans*) appears, with exostoses, osteoporosis, osteosclerosis, fibrillation and atrophy of cartilage, ecchondroses, sometimes combined with villous proliferation, lipoma arborescens, etc. Such deforming changes are occasionally met with at the end stage of an alterative, or of an exudative, inflammation of long standing (*secondary arthritis deformans*), but such changes appear more often, and more characteristically, as a process *sui generis,* productive from the first, with marked lipping of bones at the edge of the articular cartilage (*primary arthritis deformans; osteo-arthritis deformans; hypertrophic osteo-arthritis*). Among the subvarieties of the latter are included (1) hypertrophic osteo-arthritis of the spine (*spondylitis deformans*), and (2) senile osteo-arthritis of the hip joint (*malum coxae senile*).

In the third form of chronic productive arthritis are included the infectious granulomatous inflammations of the joints (*tuberculosis, lues, leprosy, actinomycosis*).

### ii. Etiological Grouping

Recently, etiological determinations have more than ever before been reflected in the terminology of the chronic joint diseases, but our knowledge is as yet far too limited to permit us satisfactorily to classify all joint lesions on this basis.

A. Names depending upon the mode of access of the pathological stimulus to a joint system.

1. Injury from the outside (*traumatic arthropathy*).
2. Injury through the blood (*hematogenous arthropathy*).
3. Injury through the lymph channels (*lymphogenous arthropathy*).
4. Injury through the nerve paths (*neural arthropathy*).

B. Names depending upon the particular variety of injury or upon the special form of abnormal stimulus concerned.

1. Physical stimuli (*traumatic arthritis, static arthritis* of Preiser).
2. Chemical stimuli (*toxic arthropathies* such as *arthralgia saturnina*).
3. Biological stimuli (as in the *infectious arthropathies*).

C. Names based upon the disposition of the joint system or of the organism as a whole to disease.

1. Based upon predisposing age (as in *malum coxae senile*).
2. Based upon predisposing conditions of poverty (as in *poor man's gout,* or *arthritis pauperum*).

### iii. Clinical Grouping

For the present, the following groups seem most useful:

1. The true chronic *gouty* arthritis.
2. The (primary) *hypertrophic osteo-arthritis.*
3. The secondary *chronic infectious arthropathies* following various bacterial invasions.
4. The so-called *primary chronic progressive polyarthritis,* in reality, a special member of the preceding group.

In connection with these four main groups, several special conditions have also to be considered:

(*a*) The villous arthritis of Goldthwait.
(*b*) The chronic arthropathies of the spine.
(*c*) Still's disease.
(*d*) Heberden's nodes.
(*e*) Bouchard's comptodactylie.
(*f*) Subcutaneous fibroid nodules.

The joints in nervous diseases are described in a special section.

#### *1. The True Chronic Gouty Arthropathy*

Reference to this, and to the metabolic process underlying it, will be found in the chapter on Gout. This form of chronic arthropathy is usually easy to recognize, at any rate in the typical cases.

The heredity, the acute exacerbations, especially as nocturnal attacks, the presence of tophi, the sites of predilection, the increased amount of uric acid in the blood (Garrod, Magnus-Levy), and the deficient purin tolerance (method of v. Noorden and Schliep, 1905), suffice for the diagnosis. In atypical cases, there may, however, be some difficulty in distinguishing the disease from atrophic or infectious forms of arthritis. The x-ray findings in a gouty joint are sometimes distinctive (spherical foci in the bone substance near the joint), or often in the form of a

semicircular defect of the articular surface of a bone with sharp, punched-out margins; if such a lesion be present in a joint of one foot there is often a similar lesion in the same joint of the other foot.

### 2. *Primary Hypertrophic Osteo-arthritis*

### (*Osteo-arthritis hypertrophicans; Osteo-arthritis deformans*)

This is easily recognizable. Though most often met with in *advanced life,* the same or a similar malady may occur in youth, especially after slight trauma.

One joint is chiefly affected, or several joints (usually only a few) may be involved. The *mono-articular,* or *oligo-articular,* distribution is in marked contrast with the more general poly-articular distribution of groups (3) and (4).

Fig. 515.—Osteo-arthritis deformans of the Knee Joint. (After F. Umber, "Lehrb. d. Ernährung u. Stoffwechselkrankh.," published by Urban & Schwarzenberg, Berlin.)

The *large proximal joints* of the extremities are most often involved (hips, shoulders, knees). There is an *absence of the steady progression* characteristic of (4). Both sexes are affected, *males* predominatingly. The general health may be but little disturbed. The disease does not lead to true ankylosis, though the joint movements may be somewhat limited through interlocking of *exostoses.* On palpation, *lipping* of the bone at the edge of the cartilage may be sometimes made out. *Free bodies* are common.

In *röntgenograms,* the joint slits are often well preserved though the cartilage may be eroded, accounting for the *grating* that may be palpable on movements of the joint; the joint slits do not entirely disappear as in (1) and often in (3). As the joint cavity is not obliterated, if oxygen be injected (method of Werndorff and Robinson) the capsule unfolds well, showing the absence of extensive adhesions and of shrinking. The presence of extensive osteophytic outgrowths, or of marked marginal lipping in the x-ray plates, especially when the clinical symptoms have been slight, is characteristic. *Static disturbances,* leading to pathological incongruence of the articular surfaces, and a history of *trauma* are common in

these cases. The disease is often asymmetrical. Among the monoarticular forms, the so-called *malum coxae senile* is included. One of the spinal arthropathies (*spondylitis deformans*) appears to belong in this group.

### *3. Chronic Arthritis Secondary to Infectious Processes (Chronic Infectious Arthritis)*

**Occurrence.**—Since septic processes have been carefully studied by bacteriological methods and their joint complications have been found to be toxic infectious processes due to the arrival in the joint, by way of the blood stream, of some of the bacteria causing the general sepsis, the idea of an *infectious origin* of arthropathies has proved to be an illuminating conception. By far the majority of acute, febrile, non-traumatic arthropathies are now believed to be infectious in nature. In many instances the bacteria have been grown in pure culture from the inflammatory exudate in the joint. As examples of bacteria thus found responsible, may be cited (1) the gonococcus (in *polyarthritis gonococcica* following gonorrheal infection of the urethra, or of the coniunctiva), (2) the pneu-

Fig. 516.—Chronic Infectious Arthritis; Hyperextension at Proximal Finger Joints. (Med. Service, J. H. H.)

mococcus (in *polyarthritis pneumococcica* complicating lobar pneumonia), (3) the streptococcus (in *polyarthritis streptococcica* complicating erysipelas, streptococcal angina, puerperal infection), (4) the staphylococcus (in *polyarthritis staphylococcica* as a part of general staphylococcus sepsis), and (5) the meningococcus (in *polyarthritis meningococcica* complicating epidemic cerbrospinal meningitis). Now, since these acute infectious (hematogenous) arthritides of definitely determined bacterial origin sometimes end neither in death nor in early recovery, but in a *chronic process* in the joints (*e. g.*, chronic gonococcal arthritis), the idea

of an infectious origin for many of the chronic arthropathies has gained credence (Bannatyne, Charrin, Chauffard, Goldthwait, Schüller). The notion was soon extended to various chronic arthropathies in which, despite the absence of demonstrated bacterial causation, the local processes in the joints and the state of the rest of the body (slight *fever,* slight *leukocytosis,* secondary *anemia, enlargement of the lymph glands,* slight foci of *local infection elsewhere*) make the assumption of a continuous (or occasionally recurring) bacteriemia of low grade with joint deposition seem possible and plausible (Allchin, Baer, Cave, Goldthwait). Under this heading come the severe forms of arthritis occurring in childhood (*Still's disease*).

At the present time, the term "infectious arthritis" is used in a very loose way. It has been made to refer to (1) the arthropathies in which bacteria have been actually demonstrated in the diseased joints, especially in the infectious granulomata (tuberculosis, lues, lepra) and in those complicating the septicemias, (2) the arthropathies that appear obviously as complications, or as sequels, of diseases believed to be infectious, no matter whether the causal agent is demonstrable in the joints or not (*e. g.,* acute rheumatism; arthritis after influenza), no matter whether the joint disease is supposed to be due to the same cause as the primary disease or to a secondary invader[1] (*e. g.,* arthritis after dysentery), no matter whether the germ of the primary disease is known or not (*e. g.,* arthropathies associated with or following scarlet fever, mumps, etc.), and no matter whether the assumed toxic infectious process affects the joints directly, or indirectly through the mediation of trophic nerves (according to the views of some regarding so-called atrophic arthritis and primary chronic progressive polyarthritis). Obviously, here, vagueness passes the permissible and a judicious restriction of the term "infectious arthropathy" seems desirable. Whether we should with the rigid restrictionists, limit its use to arthropathies in which bacteria are actually demonstrable in the joints, or should extend it to include the arthropathies that may reasonably be supposed to be due to local bacterial deposition, though such deposition cannot yet be demonstrated, is open to discussion. We do not hesitate to regard scarlet fever and measles as acute infectious diseases, though their microbic origin still awaits demonstration, and, personally, I cannot help feeling it legitimate to designate as "infectious" the arthropathies like those of acute rheumatic fever, and those chronic types growing directly out of acute or subacute processes associated with fever, leukocytosis, and enlarged lymph glands. But, pending further investigations, it does seem desirable when differentiating the arthropathies on etiological grounds, carefully to distinguish (1) the *demonstrably infectious* from (2) the *probably infectious,* (3) the *possibly infectious,* and (4) the *certainly non-infectious.* We should also, when using the term "infectious," keep clearly in mind the difference between (*a*) an infection demonstrable in a joint-system itself, and (*b*) an infection somewhere in the organism as a whole, with secondary infectious or non-infectious changes (toxic, nutritive; trophic) in a joint-system. I emphasize this point because of the great importance, in the chronic arthropathies, of minute foci of infection distant from the

[1] It would seem that many of the cases described as Poncet's disease (*rhumatisme tuberculeux*) are really instances of infectious arthritis of unknown origin occurring in persons suffering from tuberculosis rather than metastatic tuberculous infections of the joints.

joints and of their removal as a therapeutic measure. Chronic inflammations of the paranasal sinuses (including the antrum of Highmore), chronic tonsillitis, chronic otitis media, pyorrhea alveolaris, alveolar abscess, chronic bronchitis, chronic ulcerative enteritis, chronic appendicitis, cholecystitis, chronic pyelitis, chronic cystitis, chronic urethritis, spermatocystitis and prostatitis, chronic salpingitis, and chronic endometritis may be mentioned among the many possible foci whence influences injurious to the "joint systems" of the body may emanate, and this without prejudice as to whether these influences are (1) *metastatic infectious,* (2) *toxic,* (3) *neurotrophic,* or (4) *noxious in still other ways.*

Much interest has been shown in the possibility of an infectious origin for the so-called "primary chronic progressive polyarthritis" (see below) or "rheumatoid arthritis" of Garrod. The mode of onset in certain cases, the course, and the x-ray changes have made many believe that this terrible disease is due to a chronic infectious process involving joint after joint. Though bacteria have from time to time been described in the joints, the findings of the observers are discordant. If the malady be a specific infectious disease, the future will have to determine the microörganism responsible, the portal or portals of entry into the blood, and the important predisposing factors. The possibility that this disease may be due sometimes to one microörganism, sometimes to another, must also be kept in mind. For, though the clinical and pathological changes are so uniform that they suggest a single specific cause, our experience with meningitis, pleuritis, etc., has taught us to await actual knowledge before attempting to close a discussion.

**Diagnosis.**—It is well to think first of the chronic arthropathies due to infectious granulomatous processes (*tuberculosis, lues,* etc.). Here the white swelling (*tumor albus*) of Wiseman, a suppurating fistula, the anamnesis, the presence or absence of lesions elsewhere in the body due to the primary disease, the study of x-ray plates (destructive processes in tuberculosis, subperiosteal swellings, regular or irregular in outline, in lues), the Wassermann reaction, and the tuberculin tests may help to clear up the diagnosis. After lues and tuberculosis have been excluded, the anamnesis may be gone into very carefully with reference to a history of a *preceding acute infection,* either of the joints themselves or of other parts of the body. One tries to determine whether or not the chronic arthropathy has followed a true acute articular rheumatism or one of the so-called acute infectious pseudorheumatisms (*vide supra*). It is clear from our examination of many of the cases recorded in the bibliography as "chronic rheumatic arthritis" following acute articular rheumatism, that the authors were in reality not dealing with a chronic arthritis following this affection (in the narrower sense) at all, but with a chronic arthritis following some one of the various other forms of acute infectious arthritis. Cultures from the blood or from the joint fluid, complement-fixation tests, and tests for bacteriolysins, agglutinins, etc., may occasionally be of help.

This study may be followed by a *systematic physical examination* in which the various *possible primary foci of infection,* mentioned in a preceding paragraph under infectious arthritis, are sought for. The search

for intracellular Gram-negative diplococci in "milkings" from the prostate and urethra in the male, or from Bartholin's glands, the urethra, and the secretions from the cervix uteri in the female, and a thorough examination of the nose and of the paranasal sinuses utilizing the methods of transillumination and of x-ray examination of the sinuses, should here form a part of the regular routine. The presence or absence of pyorrhea alveolaris, of antrum disease, of abscesses at the roots of the teeth (x-ray), of chronic tonsillar infection (palatine or pharyngeal), and of chronic otitis media, should be determined. If the case be seen in the later stages, a marked asymmetry of the joints affected, an absence of steady progression, or the complete ankylosis of single joints, may speak for a chronic arthritis secondary to some infectious process rather than for the so-called primary chronic (progressive) polyarthritis.

Fig. 517.—Chronic Infectious Arthritis. Dislocation of Thumb at Interphalangeal Joint. (Med. Service, J. H. H.)

In the x-ray plates of these cases it is common to find disappearance of the joint slits, atrophy of the cartilages, softening and distortion of bones, and occasionally telescoping.

### *4. The So-called Primary Chronic Progressive Polyarthritis (Rheumatoid arthritis of A. E. Garrod; Polyarthritis destruens of Hoffa; Rhumatisme chronique d'emblée of French writers)*

This is of all the chronic arthropathies the most malign.

Clinically, primary chronic progressive polyarthritis (4) may appear as either one of *two subvarieties.* In both of these, the involvement is outspokenly *polyarticular,* the small distal joints of the fingers, toes, wrists, and ankles, usually being involved first. Later, the knees and elbows may become involved; the hips and shoulders frequently escape. These *small joints* become involved *symmetrically.* The jaw joint and the sternocla-

vicular joint are not infrequently affected, and, strangely enough, usually asymmetrically. Some of the cases of ankylosing spondylitis (*vide infra*) belong to this category.

In *one subvariety* (a) the disease may begin either insidiously or with an acute, or subacute, stage, with fever; in both forms of onset a striking feature is the *periarticular swelling*. Each joint of the proximal row of the joints of the fingers (with the exception of the thumb) often presents a spindle-shaped or fusiform appearance and feels elastic when compressed between the thumb and forefinger of the examiner. Most of the small joints in the distal parts of all four extremities may become affected in serial sequence. It is often impossible in the early stages to decide whether we are dealing with a true chronic progressive polyarthritis of group (4) or with one of the serious maladies of group (3).

In the *second subvariety* (b), most often met with in women near the menopause, the onset may be very insidious. The patients complain first

Fig. 518.—Chronic Progressive Polyarthritis, or Rheumatoid Arthritis. (Med. Service, J. H. H.)

of formication, of chilly feelings, and of *slight stiffness* of the metacarpophalangeal and interphalangeal joints (except those of the thumb). *Muscular-atrophy* quickly appears, especially of the interossei. *Contractures* gradually develop. The disease spreads to a large number of the more distal joints in all four extremities. The *fingers become deflected* ulnarward. The hands may present the "flexion type" or the "extension type"

of Charcot, or the "straight" type, but these do not represent essential differences and are unimportant for classification. On x-ray examination the joint slits are found to have disappeared owing to *atrophy of cartilage,* the *bones* are softened, and may have undergone distortion or *telescoping,* and they are usually markedly *atrophic*—so-called "atrophic arthritis" of Goldthwait (*vide supra*).

The subvariety (a) is sometimes called the *exudative type;* it is the "periarticular type of arthritis deformans" (in part) of T. McCrae, and corresponds to the "nodosities" of Haygarth, the *rhumatisme noueux* of Trousseau, the "arthritis nodosa" of Schuchardt, and the "chronic infectious arthritis" (in part) of Goldthwait.

The subvariety (b) is the so-called *dry form,* and corresponds to the "atrophic arthritis" of Goldthwait, the "atrophic type of arthritis deformans" of T. McCrae, and the *arthrite sèche* (in part) of French writers.

The subvariety (a) can certainly be simulated by chronic gonorrheal polyarthritis; x-ray plates will not distinguish between them. In lues hereditaria tarda an arthropathy similar to subvariety (a) is sometimes seen, but it should not be difficult to exclude it (Hutchinsonian teeth, keratitis, positive Wassermann, luetic changes in x-ray plate at epiphyseal line).

The absence of endocardial and pericardial changes in "primary chronic progressive polyarthritis" is striking when contrasted with the findings in acute rheumatic fever, the acute pseudorheumatisms, and in the chronic infectious arthritides.

It cannot be too strongly emphasized that subvariety (b) is often (some think always) an end stage of a condition beginning as subvariety (a). It seems to me certain that, later on, group (4) will not be considered separately, as a disease *sui generis,* but will be placed in group (3). It may be that the clinical appearances described as (4) may follow upon a variety of infections, but for the present, the weight of evidence seems to me to favor the view that (4) is really a disease of unknown, though unitary, infectious etiology.

### 5. *Certain Special Joint Conditions*

Before leaving the arthropathies a few words must be said concerning several special articular conditions.

**Chronic Villous Arthritis.**—This form of "dry joint" is believed by Goldthwait not to be a general disease at all but a local process entirely, with no tendency to progression, characterized by an absence of general symptoms, by crepitation or creaking of the joint on motion, with varying degrees of pain and tenderness on movement. It is most commonly met with in the knee as the result of flat-foot. This type appears to be one of the "static arthropathies" of Preiser. It probably corresponds in Hoffa and Wollenberg's classification to "chronic irrita-

Fig. 519.—Chronic Spondylitis deformans or Osteo-arthritis hypertrophicans. (After Pastine, "Nouvelle iconographie de la Salpêtrière." published by Masson et Cie, Paris.)

tive arthritis." It seems likely that it may follow the action of irritant causes of different kinds.

**Arthropathies of the Spine.**—The subject is difficult to deal with in a few words. The most important point to emphasize is, it seems to me, the fact that the joints and bones of the spine are subject to diseases precisely in the same way as the other joints of the body. We meet in the spine with (1) the gouty, (2) the neuropathic (tabetic), (3) the hypertrophic osteo-arthritic, (4) the secondary chronic infectious, and (5) the primary chronic progressive forms. Anatomically, aside from traumata, the neuropathic arthropathies and the infectious arthritides of the spine (tuberculosis, lues, gonorrhea, typhoid, etc.), which usually affect the spine locally rather than throughout its whole extent, two main processes seem to occur in the vertebral column: (1) a hypertrophic osteo-arthritis of the spine (*spondylitis deformans*), and (2) a chronic ankylosing arthropathy of the spine (*spondylitis chronica ankylopoietica*).

Fig. 520.—Röntgenogram of Spine Illustrating Spondylitis ankylopoietica (Marie-Strümpell type). Note the Ossification of the Lateral Ligaments. (X-ray Dept., J. H. H.)

In hypertrophic osteo-arthritis of the spine **(spondylitis deformans)** the process seems to begin in the intervertebral disks; there are marked exostoses on the bodies of the vertebra and, especially, "lipping" of the vertebral bodies at the edge of the intervertebral disks, often with a few clasplike formations extending from vertebra to vertebra, but never so extensively as in the ankylosing forms. The small joints between the articular processes never undergo intracapsular ankylosis in this disease, though motion may be limited by exostoses. The nerve roots may be compressed. The disease occurs chiefly in advanced life. It almost never causes complete rigidity of the thorax.

In **spondylitis chronica ankylopoietica,** the disease begins in the small joints of the articular processes and quickly leads to ankylosis; the costovertebral articulations are often involved also. The ligaments of the spine sometimes become ossified, but many of the bony bridges or clasps uniting the vertebrae may be independent of the ligaments. Of this chronic ankylosing spondylitis, two clinical

forms have been described: (1) the **"Marie-Strümpell subtype"** beginning below and extending upward, described by Marie as *spondylose rhizomélique,* on account of the simultaneous involvement of the articulations of the vertebral column and the proximal joints of the extremities (hips, shoulders); and (2) the **"Bechterew subtype"** with outspoken kyphosis of the upper thoracic spine, the process beginning above and extending downward.[1] Later studies (Fraenkel, Simmonds, Janssen, Anschutz, Plesch) have shown that all sorts of transitions exist between the Bechterew type and the Strümpell-Marie type; these two subtypes do not represent anatomically separable processes in the spine. Rigidity of the spine is easily recognizable clinically. Pains in the spine, radiating into the trunk or the extremities, stiffness gradually extending to all movements of the spine, with a tendency to kyphosis, are characteristic phenomena.

The differential diagnosis between spondylitis deformans and the ankylosing variety is, in most cases, easily made. If the breathing be wholly abdominal owing

Fig. 521.—Scheme Showing the Different Attitudes and Modifications of the Figure from Deformity of the Spine, and Ankylosis, in Flexion, of the Hips in Cases of "Spondylose rhizomélique." The Height of all the Subjects Measured from Head to Foot following the Contour of the Vertebral Column, Is Supposed to be Equal to that of a Normal Subject. The Portions of the Limbs That Are Still Movable Are Marked in Dotted Lines. (After P. Marie, "Exposé des Titres et Travaux Scientifiques," published by Masson et Cie, Paris.)

to ankylosis of the costovertebral articulations or to the general approximation of the origin and insertion of the accessory respiratory muscles from kyphosis or from stiffness of midthoracic spine, or if the disease occur in young persons, under 40, it is almost certainly chronic ankylosing spondylitis. The spine is more uniformly involved throughout its whole length in the ankylosing type than in spondylitis deformans. Röntgenograms are decisive in most cases. As to early cases, in spondylitis deformans the bone changes may be marked and the clinical symptoms slight, while in the ankylosing spondylitis severe clinical symptoms may precede demonstrable bone and joint changes by a year or longer.

**Still's Disease.**—This disease, a chronic arthritis of childhood, described by G. F. Still (1897), probably represents neither a clinical nor an etiological unity. In Still's disease we appear sometimes to deal with a secondary chronic infectious arthritis (3) and sometimes with a primary chronic progressive polyarthritis (4).

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[1] A few of the cases described clinically as Bechterew's type turn out on x-ray examination to be spondylitis deformans.

The presence of a large spleen, large lymph glands, leukocytosis, and secondary anemia are strongly suggestive of chronic infection.

**Heberden's Nodes.**—These nodes are due to excrescences on the base of the terminal phalanges of the fingers. They are easily recognizable on inspection, on palpation, and in the x-ray. In my experience they occur most often in association with chronic hypertrophic osteo-arthropathies, though they are sometimes seen in gout, and they sometimes occur as an isolated phenomenon, not associated with arthritis of the other joints. In the x-ray the adjacent joint may be but slightly affected, or, in some cases, the joint may show changes like those in primary chronic progressive polyarthritis. Heberden's nodes cannot, therefore, be said to be pathognomonic of any one form of chronic arthropathy; indeed they seem to occur in connection with several different forms, and by themselves. It would seem probable that Heberden's nodes do not represent even a morphological unity. They appear sometimes to be true exostoses (in hypertrophic osteo-arthritis), sometimes to be projections due to softening and flattening of the base of the terminal phalanx (in infectious and in chronic progressive arthritis), and, finally, sometimes to be nodules due to gouty changes in the bones. Dr. W. S. Baer tells me that even on palpation varieties of Heberden's nodes are distinguishable: certainly in röntgenograms a variety of structures can be made out in the different types of cases.

**Bouchard's Comptodactylie.**—Bouchard has described fusiform swellings of the proximal finger joints as an accompaniment of dilatation of the stomach; they are said to disappear when the stomach lesion is cured. Přibram has seen one such case. I have not observed this relationship. The relation of chronic arthritic affections to various disturbances of the digestive tract has been emphasized by Coutaret and also by Goldthwait (in visceroptosis).

**Subcutaneous Fibroid Nodules.**—These little bodies attached to the tendons and fasciae (Meynet, Barlow and Warner, T. B. Futcher, Hawthorne) may occur in almost any form of chronic arthritis. They were at one time supposed to be pathognomonic of true "rheumatic" affections. They are not to be confused with the *nodosités cutanées éphémères* of Fereol.

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## 5. The Neuropathic Arthropathies

(*Charcot's Joint*)

**Occurrence.**—In *tabes,* in *syringomyelia* and in other chronic diseases of the spinal cord, or of the peripheral nerves, peculiar joint-changes

occur, which since Charcot's time have been understood to depend upon neural lesions.

**Diagnosis.**—These forms will not easily be overlooked if, in addition to the examination of the joints, a thorough neurological examination be made (tests of sensibility, knee-kicks, pupils, etc.).

Fig. 522.—Röntgenogram of Ankle; Charcot's Joint. Arrows Point to the Marked Destruction of the Tarsal Bones. (X-ray Dept., J. H. H.)

Moreover, the sudden onset, the marked enlargement of a single joint, and the absence of severe pain, are characteristic. Astounding changes are made visible by the x-ray; bizarre, monstrous hypertrophic lesions predominate; besides excrescences upon the bone and huge calcified free bodies, calcified masses are usually visible in the extracapsular tissues; some regressive (atrophic or absorptive) changes are also present and there is usually extreme disintegration of the joint.

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# Part XII

# Diagnosis of Diseases of the Nervous System

Section I

METHODS OF EXAMINING THE NERVOUS FUNCTIONS (THE ACCUMULATION OF DATA)

## A. Introduction

Since it is chiefly differences in the structure and in the functions of the nervous system that explain differences in capacities among the higher animals, inclusive of man, a careful study of this system must always be important for pathology, and especially for human pathology. The functional activities of lower animals are simpler than those of higher animals, mainly because their nervous systems are less complex. The dominance of man among mammals depends mainly upon the architecture and capacities of the anterior end of his nervous system, the cerebrum. Indeed, the main differences among human beings themselves, the fine qualities that distinguish men and women from one another, are doubtless, likewise, in large part, the result of variations in brain structure and in brain power. Euclid was a different man from Shelley, Edmund Spenser from Herbert Spencer, King David from David Hume—to choose as striking examples the same names as those selected by Professor Walter Raleigh to illustrate differences in style. We have already begun to gain an insight into differences that count. But though the foundations of the study of the nervous system and its functions are already laid, the buildings thus far erected upon them have been purely temporary in character, to be replaced during our lifetime and in the lives of those that succeed us by higher and better arranged structures. We can be sure that, in the future, physicians will pay much more attention to the functions of the brain and other neural organs than they do now.

For the clinician, neurology and psychiatry must always rank as most important chapters of internal medicine. Though they are, and laudably, cultivated also as special disciplines, their relations to internal medicine as a whole are so intimate that a general internist, on the one hand, must fail in his work if he be unacquainted with their aims and methods, and the neurological and the psychiatric specialists, on the other, can have become really expert only after a thorough training in internal medicine. It is especially through the autonomic nerves, that the cerebrospinal nervous system is thrown into most intimate connection with the various vital organs. Through them the secretory processes of the digestive glands (salivary, gastric, intestinal, etc.), as well as the secretory activities of the organs that separate the urine, the sweat and the milk, are profoundly influenced by what goes on in the nervous system. The work of the heart stands directly under the influence of the autonomic fibers of the vagus and the accelerator nerves, and the distribution of the blood in the body is continuously undergoing alteration through changes in the caliber of the vessels in different parts, dependent upon the activities of the vasomotor neurone systems. In respiration, further, a neuromuscular mechanism is utilized in which the vagus, the phrenic and certain other peripheral nerves play a part; its rhythmical nature depends upon chemical stimulation of the cell bodies of the neurons situated in the so-called "respiratory center" in the formatio reticularis. The propulsion of food through the digestive canal, the emptying of the secretions from the digestive glands by contraction of the smooth muscle in the walls of their ducts, the muscular activities of the ureters and bladder and of the system of genital ducts in both sexes, are subordinate to accurately regulating neural impulses. Finally, the nutrition of the body as a whole is in part consequent upon the workings of the nervous system; thus the state of nutrition of the muscles, the carbohydrate metabolism, the nitrogen metabolism, the heat regulation, the deposition of fat, the growth of bone—all are, in part directly, in part indirectly through the intervention of the glands of internal secretion, dominated by the nervous system. Surely, therefore, the physician should be as familiar with the methods of examining the nervous system as he is with those for examining the lungs, heart, kidneys, stomach and metabolic organs! And the neurologist and psychiatrist unacquainted with the general methods of internal medicine would be sadly at a loss in understanding and interpreting many of the phenomena met with in their special fields. The relations of lead colic to saturnine encephalopathy, of air hunger to diabetic coma, of acute infection to febrile delirium, of hyperthyroidism to so-called neurasthenic and psychasthenic states, of arterial hypertension and atherosclerosis to certain forms of encephalopathy, and of contracted kidney and uremic poisoning to disturbances of consciousness, may be cited as examples.

The methods of examining the nervous system and its functions

clinically are for the most part simple and easy to learn. The technic of a thorough examination of the functions of the nervous system, aside from psychiatry, can be, under skilled instruction, acquired in a short time. Psychiatric methods of examination are more difficult and as yet they have been very incompletely elaborated, but the more important methods of psychiatric inquiry can also be easily and quickly acquired.

But while the methods are not complex or difficult to learn, the interpretation of the data accumulated by applying them presents difficulties due chiefly to the undeveloped state of knowledge regarding the functions of the nervous system. Interpretation of results, as far as such interpretation is at present possible, is in reality not difficult, provided the facts of the anatomy and physiology of the nervous system, as thus far worked out, are understood and appreciated. There are perhaps no other departments of medicine that, for the interpretation of clinical findings, require so thorough a foundation in anatomy and physiology as do neurology and psychiatry. The anatomy of the nervous system is singularly complex and until recently very few medical schools have made provision for the thorough training of students in it. Moreover, even when the opportunities for such training are offered there are many students who seem unable to prolong the stretch of attention necessary to get a grasp of the architectonics of the nervous system and of the neural activities, or who, for some reason or another, seem to be devoid of that capacity for thinking in three dimensions that the study of conduction paths within the central nervous system makes imperative. When we realize further that only a few students entering medicine have received any training in normal psychology, and recollect how important an analysis of the mental factors is for the appreciation of psychoneurotic and psychiatric states, it is but little wonder that, hitherto, the majority of medical students have fought shy of the serious consideration of the psychic state of their patients, regarding it as outside the domain of general medicine, a field entirely for cultivation by specialists. The time for a persistence in this attitude now seems past; the general practitioner who, from now on, fails to secure a training, at least in the fundamental methods of neurologic and psychiatric study, will be seriously handicapped.

The study of a patient on the neurologic and psychiatric side consists in (1) the *accumulation of data* concerning the neural and mental state, (2) the drawing of inferences regarding the *site of the disease process*, and (3) the formation of conclusions regarding the precise *nature of the process*.

Satisfactorily to *gather data* concerning the neural and mental state, the functions of the nervous system must be subdivided into groups (analysis), and each group tested for itself; during this gathering process, the examiner should keep his mind free, as far as possible, from preconceived opinion regarding the site and nature of the lesions present.

After the methodical testing of the various functions has been completed, the facts gathered should be considered as a whole. In deciding upon the *site of the lesion,* its localization within the great complex of neurons that makes up the nervous system as a whole, one considers especially (a) the topographical distribution of the abnormal phenomena met with, and (b) the character of the deviations from the normal.

In forming conclusions regarding the *nature of the pathological process* present, one tries to decide, (a) whether it is "organic" or "functional" in its nature, and (b) from the totality of the symptoms and signs, and from a consideration of their suddenness or slowness of onset, their sequence, their accompaniments in other parts of the body, and the possible etiological factors, exactly how it has developed.

The cerebrospinal and sympathetic nervous systems taken together are composed of a mass of single cell-units or neurons, united with one another, through synapses, into a continuum. This continuous mass of nerve cells is incessantly, throughout life, in a state of greater or less activity. In sleep the activities appear to be reduced to the minimum required for the maintenance of the vital functions; during waking hours the activities are markedly increased, though not uniformly, throughout the mass, great groups of neurons, now here, now there—centripetal neuron systems, centrifugal neuron systems, associative neuron systems, lower reflex arcs, higher instinctive mechanisms, "voluntary" mechanisms under the influence of attention—flashing into activity in response to the influences of the outside world or to changes occurring within the body itself. In subdividing the functions of the nervous system into groups for the special purpose of clinical examination, we choose methods that will permit us to test the more important functions quickly and simply. These are methods of observation and of simple experiment. On the observational side we note the spontaneous motor and psychic manifestations of the patient and also any vasomotor, trophic or secretory phenomena visible. On the experimental side we apply (1) various methods that experience has shown will affect the consciousness of normal patients and we ascertain whether the patient yields normal or abnormal responses (objective examination of the psyche and of the sense organs), and (2) certain methods that reveal alterations in the neurons concerned in motility and in reflex action (objective examination of motility, coördination, reflex action, etc.).

The nervous system develops as a series of segments, each segment consisting of reflex arcs composed of synapsized sensory and motor neurons, the segments gradually becoming united so as to permit of larger and larger reflex mechanisms and greater and greater associations among them, until, finally, in the brain, enormous groups of associated neurons come to lie between the receptive or afferent side on the one hand, and the expressive or efferent side, on the other. For purposes of clinical anal-

ysis it is easiest, at present, to study first the receptive or afferent side as a whole, secondly the effective or expressive side as a whole, and lastly to make a special examination of particular mechanisms, reflex, instinctive and associative, which make use of portions of the afferent and efferent paths in common. We proceed, therefore, in our technical examination to study:

(1) The functions of the afferent paths (testing of sensation and of other functions dependent upon centripetal impulses).

(2) The functions of the efferent paths (testing of motility, including the reflexes and active and passive movements and the movements in organs supplied by autonomic nerves, and the examination of secretory and trophic functions).

(3) The functions of the higher associative neuron systems (testing the higher coördinated activities, especially speech, writing and the mental functions).

(4) Conditions accessible to certain special methods of examination (anthropological methods, x-ray examinations, examination of fluid obtained by lumbar puncture, electrodiagnostic methods).

(5) The localizing diagnosis.

(6) Finally, the exact nature of the pathological processes present (special pathology).

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# B. Examination of Sensation and of the Afferent Conduction Paths

## 1. The Multiple Functions of the Afferent Receptive or Centripetally Conducting Neuron Systems

Beginning in the skin, mucous membranes and internal organs of the body and in the organs of special sense, are the peripheral processes of the peripheral centripetal neurons, exposed to local stimuli in all these various parts; here impulses start that are carried into the central nervous organs. On arrival there they are, according to their quality and intensity, variously distributed, following different but definite paths. Some of them, transferred chiefly through collaterals, influence the peripheral motor neuron systems (lower reflex arcs); others, through shorter and longer paths, influence centrifugal neurons of the second and of higher orders, and have to do with complex mechanisms like those controlling the instinctive reactions, the respiratory and vasomotor neuron systems, the neuron systems maintaining body equilibrium, the neuron systems underlying the emotions, the various neuron systems coordinating the more complex bodily movements, etc. And still others traverse the longer centripetal paths composed of superimposed sets of

neuron systems, so as finally to reach the so-called sensory areas of the cerebral cortex, where they cause changes that are associated in consciousness with what we call sensation. Many of the functions of these centripetally conducting neuron systems go on, therefore, below the threshold of consciousness; only part of the impulses extend far enough and are of the quality or intensity necessary to give rise to those changes that are associated with awareness.

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*Neurones within the central nervous system connecting the end stations (nuclei terminales) of the axones of the peripheral centripetal neurones with other portions of the central nervous system (centripetal neurones of the second order and of higher orders; central neurones of the sensory conduction paths). In: Nervous system and its constituent neurones. New York,* ***1899,*** *556–882.*

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## 2. Varieties (or Modalities) of Sensation

The sensations that arise in consciousness from sufficient stimulation of afferent or centripetally conducting neuron systems are divisible into two great groups: (1) those pertaining to *common or general sensibility,* arising from stimulation of the centripetal paths distributed to the skin and mucous membranes, the mesoblastic tissues and the viscera; and (2) those pertaining to the *special senses,* and having their origin in stimulation of the centripetal neuron systems distributed to the organs of taste, smell, hearing, sight and vestibular equilibratory sense. This subdivision into general or common sensibility and special sense is merely arbitrary, since certain portions of the so-called common sensibility are just as special as any pertaining to the so-called organs of special sense. The principal distinction between the two sets of sense organs consists in the greater phylogenetic antiquity of those of so-called common sensibility.

Common or general sensibility has its origin in (a) the superficial sense organs of the *skin and mucous membranes,* mediating the elementary sensations of pain, touch and temperature, and taking part in the more complex sensory and perceptive processes known as the localizing sense, the sense of space and the stereognostic sense; (b) the deep sense organs of the *mesoblastic tissues,* mediating the elementary sensations that yield information regarding posture, passive movement, periosteal pain, vibration, and the sense of muscular contraction, these being factors in the more complex sensory activities that have been described under the captions of the innervation sense, the sense of power or strength, and the

sense of active movement; and (c) visceral sense organs, mediating the sensations arising in the *viscera* and including the centripetal impulses that, when pathologically increased, give rise by a special anatomical mechanism to referred pain in domains innervated by the cutaneous nerves (sensory zones of Head).

A summary of the varieties or modalities of sensation is given in the accompanying tables:

VARIETIES (MODALITIES) OF SENSATION

I. *Common or general sensibility.*
  A. Superficial (skin and mucous membrane).
    AA. Elementary.
      (a) Protopathic system (Head).
        1. Sense of pain.
      (b) Epicritic system (Head).
        2. Sense of touch.
        3. Sense of temperature.
          (a) Warmth.
          (b) Cold.
    AB. Complex.
      (1) Localization.
      (2) Space sense.
      (3) Stereognostic sense or perception.
  B. Deep (other than visceral).
    BA. Elementary.
      (1) Sense of posture and of passive movement.
      (2) Periosteal sensations (pain and vibration).
      (3) Sense of muscular contraction.
    BB. Complex.
      (1) Innervation sense; sense of power or strength.
      (2) Sense of active movement.
  C. Visceral.
II. *The Special Senses.*
  A. Taste.
  B. Smell.
  C. Hearing.
  D. Sight.
  E. Vestibular.

It will be noted that certain sensations refer to the world outside the human body, and that others refer to the changes taking place

within the body itself. Besides the sensation proper resulting upon stimulation, certain sensations, if not all, have an influence upon the affective or emotional state of the person—they are pleasant or unpleasant. This quality is known as the "feeling-tone" of the sensation; thus pain is always accompanied by negative feeling-tone—it is unpleasant. Gentle thermal stimuli usually give rise to sensations accompanied by positive feeling-tone—they are pleasant.

## 3. General Remarks on the Making of Sensory Examinations

The simplest effective methods of examination should be chosen. Elaborate armamentaria have been devised, including a variety of esthesiometers and, in the domain of the special senses, of complex machines for the making of elaborate tests. All these should be avoided by the clinician in his every-day work, though they have their place in special psychological and psychiatric laboratories for purposes of precise investigation.

Besides using simple apparatus only, the examiner should follow some plan of quickly orienting himself regarding the state of a given type of sensory apparatus; should any abnormality be found the disturbance can subsequently be exactly delimited.

Certain conditions favor the making of sensory examinations; others interfere with the tests. In the first place, the patient must have sufficient intelligence to understand how to recognize sensations; imbeciles cannot be satisfactorily examined on the sensory side. Again, the consciousness of the patient must be sufficiently clear for the purpose; sensory examinations cannot be made if the patient is comatose or delirious. Furthermore, the patient must be willing to coöperate in the examination —he must manifest good will; in the negativism of dementia praecox, for example, the patient may not coöperate and, if so, cannot be satisfactorily examined. Even where there is good will, there must be a certain capacity for concentration of attention, the motor ability to respond must exist and the patient should not be fatigued. It is well to make a sensory examination, therefore, in a quiet room rather than in a general ward, to make it with the patient alone, or, in the case of a woman, in the presence only of the nurse; sensory examinations made before a ward class or in the presence of a family or group of friends are notoriously unsatisfactory. A complete sensory examination requires the expenditure of a considerable amount of time and should be undertaken only when both patient and physician are at leisure. It is frequently necessary to divide an elaborate sensory examination into two or more parts to be carried out on different occasions.

Abnormal sensibility to stimulation is known as *hyperesthesia,* enfeebled sensibility as *hypesthesia* and complete loss of sensibility to stimulation as *anesthesia.*

Besides these quantitative disturbances of sensation we pay attention to the *topographical distribution* of a sensory disturbance, attempting in every case exact delimitation; we can thus distinguish between circumscribed and diffuse lesions, unilateral and bilateral lesions. These exact delimitations will later be seen to be of great importance in deciding upon the site of a lesion, since the topography of sensory disturbances varies greatly according as the lesion is cerebral, spinal, radicular or neural in origin.

Finally, when sensory surfaces mediate different varieties of sensation (*e. g.,* skin, retina) it is essential to determine the particular qualities of sensation that are disturbed; thus, a cutaneous anesthesia may be *total,* involving all sense modalities of the skin, or it may be *partial* or *elective,* affecting only particular sense modalities; in the latter instance, the term *dissociated sensory disturbance* is sometimes used. Two main types of the latter are recognized: (1) the so-called *syringomyelic type* of sensory dissociation, in which there is loss of pain sense and temperature senses, with retention of the sense of touch and of the mesoblastic sensibility; and (2) the so-called *tabetic type* of sensory dissociation, in which there is a loss of deep sensibility and sometimes of the sense of touch, with retention of the sense of pain and the temperature senses. These elective dissociations depend either upon (1) separation of the paths for these different sense modalities within the central nervous system, so that localized lesions may affect one set of paths without involving the other, a point that will be further dwelt upon when the significance of the topography of sensory disturbances for localizing diagnosis is treated; or upon (2) a selective affinity of certain toxins for fibers mediating certain of the modalities of sensory impulses.

When a sensory disturbance consists less in loss of sensation or increase of sensation than in a perversion of sensation, it is spoken of as a *paresthesia.* Such paresthesias, however, when carefully analyzed, are usually found to be combinations of anesthesia and hyperesthesia in sensory surfaces mediating more than one variety of sensations. They are often phenomena of sensory irritation appearing without external stimulus and giving rise to continuous or intermittent sensations of unusual nature noticed by the patient. Among them may be mentioned prickling sensations, the sense of formication, the feeling as though a limb had gone to sleep (paresthesia from pressure), the feeling as though felt were under the feet in tabes, and the feeling of tension about the waist, sometimes spoken of as "girdle sensation."

The promptness of response to stimulation should always be noted. There is, normally, great difference in *reaction time,* first, for different

sense organs in the same patient, response to tactile stimuli being much more prompt than response to pain-stimulation, and, secondly, for the same sense organ in different persons. In certain diseases, however, there is marked pathological delay in response and abnormally long reaction time. In *hyperesthetic* states, when single stimuli are ineffective, the influence of a summation of stimuli should be noted.

The results of sensory examinations are of the greatest value for diagnosis. No data are more helpful in making decisions as to the site and nature of organic lesions than those derived from the testing of the functions of the centripetally conducting neurons. These data are also most helpful in distinguishing between organic disease and the so-called functional disorders. The limits of a sensory disturbance in the skin, for example, should be marked with a blue pencil, purely objectively, and subsequently transferred to charts of the body for permanent record.

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## 4. The Sense of Touch and its Anomalies

The sense of touch (slight contact or delicate pressure) is mediated in the skin chiefly by nerve-beginnings connected with the hair follicles; in non-hairy parts of the skin and in the mucous membranes the tactile sense organs appear to be Meissner's corpuscles.

### (*a*) *Touch Points*

The individual *touch points* can be sharply localized and their threshold-stimulus determined by means of von Frey's test hairs, but for ordinary clinical purposes a less delicate method of examination is used. One applies a small wisp of cotton or a dry, soft, camel's hair brush to

the surfaces to be tested. It is best to hold the eyes of the patient shut with the thumb and forefinger of the left hand and to make the tests with the right hand; or a towel may be placed over the eyes during the examination. The patient should be told to pay close attention to sensory impressions in the skin and he should be shown, before the eyes are closed, what he may expect. When a tactile sensation is felt, the patient may answer "no" or "yes" or may count as he feels the successive stimuli. The stimuli should be brief and the pressure very slight, so as to avoid stimulation of pain points or of the sense organs of the deeper tissues. Further, one should avoid applying the stimuli at regular intervals, since the patient, growing accustomed to the rhythm, may give positive answers even in the absence of sensation. It is also wise to pass, occasionally, from one part of the body to another unexpectedly.

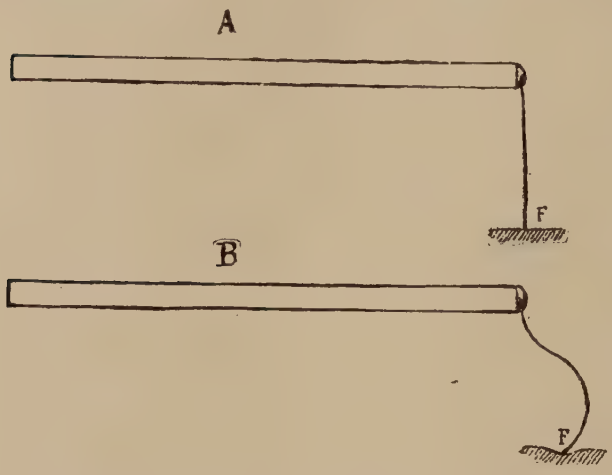


Fig. 523.—Von Frey's "Test Hairs," for the Finer Analysis of Tactile Sense. (After L. F. Barker, J. H. H. Bull.)

In the first rough examination for quick orientation it is well to stimulate in a circle around each forearm and upper arm, around each leg and thigh, and vertically downwards on each side of the face and along the middle of each half of the trunk in the front and back. Such a mode of application of the stimulus crosses the areas supplied by most of the individual peripheral sensory nerves and also the bands corresponding to the posterior nerve roots, such bands running lengthwise on the extremities and transversely on the trunk (see Topical Diagnosis). A special effort should be made to ascertain, in the absence of anesthesia, the existence of slight differences in the intensity of sensation experienced with the same strength of stimulus applied to the two sides of the body. A unilateral hypesthesia may sometimes thus become recognizable.

For exact threshold determinations of touch sense and pain sense, we make use of v. Frey's test hairs.

### (*b*) *Anomalies of the Sense of Touch*

Hyperesthesia in the domain of the sense of touch is known as *hyperpselaphesia;* diminution of this sense is called *hypopselaphesia* and loss

of it *apselaphesia.* It should be borne in mind that the sense of touch (strictly speaking) is absent in certain parts of the body (cornea, glans penis, mammilla). Most sensitive regions are the lips, forehead, back of tongue, cheeks and temples; next in order are the dorsal surfaces of the terminal phalanges, the dorsal surfaces of the forearms and the backs of the hands; the soles of the feet, and the dorsal surfaces of the lower extremities are relatively insensitive to touch.

### (*c*) *Localizing Sense*

The power to localize the point to which a stimulus is applied to the skin depends, first, upon the *local sign* pertaining to the sense of touch, the sensation from each touchpoint being distinguishable from that from any other, and, secondly, upon experience that has been gained by the sense of sight and the sense of movement in connection with this sense of touch. One tests it by asking the patient to point to the exact spot to which the stimulus (a blunt point) has been applied and removed. When we touch him, his eyes should be closed; when he tells us where we touched him, he may do so with closed or with open eyes, pointing in the latter instance to the spot touched on his own body, or to the symmetrical spot on the other side, or to the spot on a photograph or on a model. Localization is not exact, even in normal persons. Mistakes as great as 1 cm. on the hands, 2 to 4 cm. on the arms and legs, and even 6 to 7 cm. on the upper arm and thigh may be met with in normal persons. The power of localization on the face is more accurate. Accuracy of localization depends somewhat upon the intensity and duration of the stimulus.

Mistakes in localization at the first touch depend especially upon the accuracy of the patient's idea of position; in order to be sure of a failure in localization on the skin, the patient must be allowed to keep on searching for the point touched until he believes he has found it (Spearman). The distance between the point he finally indicates and the point originally touched is the measure of the fault in localization.

In pathological cases there may be marked disturbances of this localizing sense; thus a stimulus applied to the hand may be localized by the patient in the upper part of his arm. In rare cases, a stimulus applied to one side of the body is referred by the patient to a corresponding spot on the opposite side (*allocheiria*).

### (*d*) *Spatial Sense*

This is tested by means of a compass with dull, non-metallic points, which has a scale giving the exact distance between the points. It is important, in making the test, that both points shall be placed simultaneously upon the skin, since two points close together, if stimulated successively, will often be recognized as two, when, if stimulated simultaneously, a single sensation results. It is only when touch points are

a certain distance apart that stimulation of them simultaneously gives rise to two separate sensations. In other words, the *successive-threshold* differs definitely from the *simultaneous-duplicity-threshold,* or *space-threshold* (v. Frey).

In determining this space-threshold, one begins by making the distance between the compass points such that a single sensation everywhere results; the distance is then gradually increased until the two points are felt separately. One may work in the opposite way, beginning with the points far apart and gradually approximating them until the single sensation appears. The results are somewhat different in the two cases, and one should always note the method employed. Some examiners use both methods and take the arithmetical mean as the threshold.

Recently, McDougall's method has been applied clinically by Head and Holmes. By this method, the distance between the compass points is not changed during the test, but, in irregular sequence, one point alone or the two points simultaneously are applied, until, finally, ten tests of each sort have been made. A second person, not applying the compasses, notes whether a correct (1) or a false (×) answer is made, so that the examiner himself is unaware of the exact number of tests he has applied until the series is complete. An example of the record kept is as follows:

$$4\text{ cm.}\frac{1 \quad 11\times\times \quad \times 1 \quad 1\times\times 1}{2 \quad \times 1\times \quad 11\times\times \quad \times\times 1} = \frac{5\text{R.}5\text{F.}}{4\text{R.}6\text{F.}}$$

In this case the compass points were 4 cm. apart. The upper line indicates the results of the tests made with a single point, the lower line the tests made with the two points. With one point there were five right answers and five false answers. With the two points there were four right answers and six false answers. The wrong answers in the one case mean that one point was felt as two, in the other case that two points were felt as one.

In examining a given area of the skin, several such tests are made with different distances between the compass points. If in the area tested there is a great difference in results from those obtained in the symmetrical healthy area, a unilateral disturbance of spatial distinction can be assumed to exist.

Another method of testing the localizing sense and the sense of space consists in determining the distance apart in which two separate and similar stimuli can be separately felt (compass test). The method is as yet of very little clinical importance.

### (e) *Sense of Roughness and Smoothness*

This is related to the spatial sense. When a rough surface is applied to the skin but not moved over it, the spatial sense alone has to be con-

sidered, but if it be moved over the skin, then we have to consider, in addition, the capacity for perceiving intermittent stimuli.

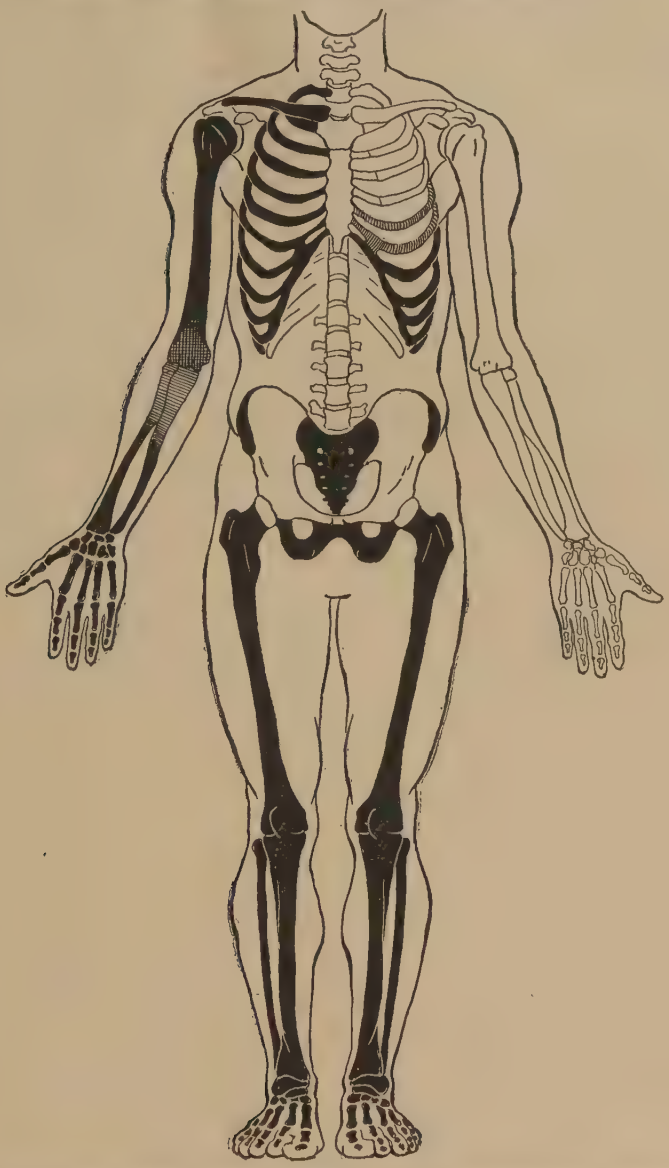

Fig. 524.—Tabes.—Diagram Illustrating Areas in Which Vibration Sense (Bone Sensibility?) Is Abolished.

For testing the threshold for roughness, Graham Brown's esthesiometer is convenient. From the smooth, convex surface of a metal cylinder six metal rods can be simultaneously shoved downward by means of a

micrometer screw. The distance to which these must be protruded in order to elicit a sense of roughness when the skin is stroked with it gives the threshold. This threshold for roughness runs fairly parallel to the space sense threshold.

### (*f*) *Vibration Sense* (*Pallesthesia*)

The touch points, when stimulated, yield sensations that are sharp, clean-cut and of short duration. If stimuli be rapidly applied, therefore, at brief intervals, separate sensations result and one gets the sensation of oscillation or vibration; thus, if a gentle faradic current be applied to the skin by means of a moist electrode used ordinarily in testing motion, the interrupter swinging free and the current too weak to cause pain, a strange sensation of vibration is, normally, distinctly felt.

The so-called sensation of vibration felt on applying a vibrating tuning-fork to the skin over the bones, and described by Eggers as a method of testing the sensibility of the bones, may be, in reality, I am inclined to think, the result of stimulation of the touch points in the skin. Though this vibration sense may disappear before there is complete tactile anesthesia, it seems to indicate that among the earlier disturbances of tactile sensation must be counted an inability to perceive successive impulses of short duration as separate sensations. The best tuning-fork for the purpose is the C-fork (128 vibrations), provided with a Gradenigo triangular block on one arm; this kind of fork permits of the application of vibrations of very different numbers and the number at the instant the sense of vibration ceases may be read off.

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## 5. The Sense of Pain and its Anomalies

### (a) *Pain Points*

The pain sense is mediated by special pain nerves (v. Frey) at particular points known as *pain points;* these are much more numerous than the touch points in the skin and mucous membranes. The sense of pain is best tested by means of a sharp needle; the patient should be taught to distinguish between the sense of pain and the sense of touch before his eyes are closed and the actual examination begun. Sometimes the examiner uses a pin, applying not alternately, but irregularly, the head or the point; the patient is required to answer the question, "Do you feel the head or the point"? or "Is this sharp or dull"? Various algesimeters have been devised, but they are wholly unnecessary for ordinary clinical work. Where the organs of pain sense have been injured, pain may yet be experienced on pinching a fold of the skin. Stronger faradic currents may also be used for testing the sensibility to pain, though, practically, one rarely applies them. Sensations of pain are very inaccurately localized even by normal persons.

### (b) *Anomalies of the Sense of Pain*

The anomalies of the sense of pain may consist in loss (*analgesia*), in diminution (*hypalgesia*) or in exaggeration (*hyperalgesia*). Promptness of response (reaction time) should be attended to, since in hypalgesias there is often delayed sensation. The effect of summation of stimuli should also be noticed, by drawing a sharp needle lengthwise over an analgesic or hypalgesic area.

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## 6. The Senses of Temperature and Their Anomalies

On the skin, temperatures similar to those of the skin itself are not felt (so-called indifferent zone). Higher temperatures are felt as warmth, and still higher temperatures as pain. Lower temperatures are felt as cold, and still lower as pain.

Thermal stimuli may, therefore, produce no sensation at all, a sense of warmth, a sense of cold, a sense of pain, or various combinations of pain sense and temperature sense.

### (a) *Warm Points and Cold Points*

Sensations of warmth are mediated by special nerves whose endings in the skin are known as *warm points.* Sensations of cold are mediated by entirely different nerves whose endings in the skin are more numerous and are known as *cold points.* The sensations of pain resulting from thermal stimuli applied to the skin are due to irritation not of the nerves of temperature sense but of the pain nerves at their pain points.

Sensations that combine a feeling of warmth or cold with pain are due to simultaneous stimulation of temperature sense nerves and pain nerves.

In testing the temperature senses, one proceeds as follows: For quick orientation one may, closing the eyes of the patient, breathe upon the skin at close range (warm stimulus), or blow upon it at a greater distance (cold stimulus); or one may use two test tubes of equal size, one containing ice water, the other warm (but not too hot) water, and apply, sometimes one, sometimes the other, to the skin, asking the patient to tell whether the tube felt is warm or cold. In comparing the response of the organs of temperature sense on the two sides of the body, it is well to apply on the two sides simultaneously test tubes containing water of the same temperature and to ask the patient whether the sensations experienced on the two sides are the same or different.

For very exact analyses of disturbances of temperature sense, where it is desirable actually to localize the single warm points and cold points at the edges of the disturbance, special apparatus may be used (Blix, Goldscheider, v. Frey).

### (*b*) *Anomalies of the Temperature Senses*

When the organs of temperature sense are abnormal, the sense of warmth and the sense of cold usually suffer together, though in rare instances the warmth nerves may be involved independently of the cold nerves. Loss of both senses is known as *thermanesthesia,* diminution as *thermohypesthesia* and exaggeration as *thermohyperesthesia.* It is to be remembered that the sudden application of heat to a cold point gives rise to a sensation of cold (paradoxical reaction of von Frey). This probably explains why one sometimes has, for a moment, a chilly sensation on entering a hot bath.

Subjective feelings of heat and cold (*ardor* and *algor*) may be due to a sudden vasomotor disturbance with rapid change in the temperature of the skin leading to stimulation of the temperature nerve endings, or they may be paresthetic disturbances in the domain of the temperature sense.

Thermanesthesia is often associated with analgesia in elective disturbance of cutaneous sensation (see syringomyelic type of sensory dissociation).

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## 7. The Deep Sensations (Bathyesthesia) Originating in the Mesoblastic Tissues

(*Sensations of Posture, Sensations of Passive Movement, Sensations of Muscular Contractions, Sensations of Active Movements, Sense of Power or Strength, Periosteal Sensations, Stereognostic Perceptions*)

The sensations having their origin in stimulation of the sensory nerve beginnings in the mesoblastic tissues (fasciae, tendons, muscles, joint-surfaces, periosteum, etc.) are of the greatest importance, since they are concerned in a whole series of complicated processes, especially in the co-ordinating of the movements of the body and in the maintenance of equilibrium; in judgments of weight and of required strength they may play an important part, and, along with the tactile sense, they are the principal constituents of our stereognostic perceptions. The totality of deep sensation, here under consideration, is designated as *bathyesthesia.* This deep sensibility is difficult of exact analysis, since the nerve beginnings in tendons, muscles, periosteum and joints are in greater or less degree simultaneously stimulated. In appreciating posture, or in judging of the

passive movements of the extremities, we rely upon the perception of differences in tension of the part mediated by the sensory apparatus of the muscles, fasciae and joints. When a single muscle is made to contract by electrical stimulation, we have a sensation of the muscular contraction; it depends upon stimulation of the sensory nerves in the muscle or in its tendons of origin and insertion during the contraction (H. Curschmann, Jr.). In the perception of active movements, we have to deal (1) with the same deep sensation originating especially in impulses arising in the joints but partly in the muscles, fasciae and tendons, and, in addition, (2) with the sensation of motor innervation, probably originating in the psychomotor centers of the cerebral cortex and not in the periphery. The same complex of sensations is in all probability involved in our judgment of weights, and of resistance to passive movement.

### (*a*) *Testing the Sense of Muscular Contraction*

In order to prevent complication with cutaneous sensibility, an arm or a leg is placed in such a position that, when the muscle to be tested contracts, there will be no friction between the skin and the surface supporting the extremity. The amount of current necessary for the minimum cathodal closure contraction of the muscle to be examined is next determined. The patient's eyes are closed and he is asked to state whether he notices a movement in the muscle tested in addition to the painful sensation of closing the current. He is told to distinguish between the feeling of contraction in the muscle itself and the sense of movement of the portion of the extremity under examination. One then sends into the muscle a series of currents, beginning with a current insufficient to cause contraction, and gradually increases the strength of the currents sent into it; the patient is asked to indicate with his finger the muscle in which the sensation of contraction appears.

### (*b*) *Testing the Sense of Posture or Attitude, and of Passive Movements of the Extremities*

We close the patient's eyes and make passive changes of position in one extremity and ask him either to describe them or to imitate them with the other. The process is repeated with the eyes open.

The sensation of the great toe joint and of the knee joint should be especially tested. We close the patient's eyes and bend the great toe slightly up and down and ask the patient to state (1) when he feels a movement in the toe, and (2) the direction of that movement. Similar tests are made with the knee joint. Any movement that the examiner can see should be appreciated by a patient whose joint sense is normal. In disease, this joint sense is often lost, or diminished in greater or less degree.

### (c) *Testing the Sense of Active Movement*

We ask the patient to close his eyes; then to move one of his extremities voluntarily in various directions, describing exactly to us what he is doing. We compare this statement with the movements actually produced. Another method is to ask the patient to look at an object near by and then, closing his eyes, to touch it with the finger, toe or heel by the shortest route.

In these tests, we must try to distinguish whether any abnormality found is due to a disturbance of deep sensation, or to a defect in the central sense of motor innervation. (See Tabetic Ataxia and Cortical Ataxia).

### (d) *Testing the Central Sense of Motor Innervation or the So-called Sense of Power or Strength*

Here we test the capacity of judging differences in the weights of bodies lifted by the extremities. We make a sling of a towel, and suspend it from the hand or the foot, and determine what differences in weight can be perceived by the patient. In employing the method one must try to separate the motor factor (central feeling of innervation) from the sensory factor depending upon the deep sensibility. The method is of very little clinical value and may be omitted by the beginner.

### (e) *Testing the Periosteal Sense*

The so-called periosteal sense or sense of vibration (pallesthesia) is in all probability not a periosteal sense proper; the tuning-fork applied over the bone is in a position in which it can best stimulate the touch-points (*q. v.*) of a considerable area of skin. The periosteum is well supplied, however, with pain nerves. As we know from surgical experience, this pain sense of the periosteum may be lost in certain diseases (tabes, leprosy, syringomyelia, etc.).

### (f) *Testing Stereognostic Perception*

Under this caption is designated the capacity of determining the form and consistence of bodies applied to the skin, especially to the palm of the hand. We usually use various coins, a lead pencil, a key, a watch, a chain, or large letters carved in wood. The process of recognition is a very complicated one, depending not only upon a complex of cutaneous sensations (touch and temperature), deep sensations, and innervation sense, but also upon the association of these in the cerebral cortex with one another into combinations known as perceptions, and combinations of these with one another and with memories of previous experiences (tactile, motor, optic, acoustic, etc.).

We find out first whether the patient can recognize the object simply laid upon his hand; if it be not so recognized, he is then permitted to move the fingers and hand so as to apply the skin with varying degrees of pressure to the object in different positions.

The stereognostic sense is especially well developed in the hand and in the mouth, owing largely to the delicate movements of the fingers and of the tongue. It is far less developed in the foot and on the trunk.

For testing the recognition of three dimensional forms, it is well to use wooden models of geometrical figures (spheres, cubes, wedges, etc.).

In the use of the terms stereognosis and astereognosis, we must distinguish between (1) astereognosis due to lesions of the sensory path to the cortex and of the primary end-stations in the cortex itself, and (2) the forms of astereognosis in which sensibility is entirely retained or only so slightly involved that the loss of stereognostic power could not be due to the anesthesia. This latter form is the so-called tactile agnosia (Wernicke's *Tastlähmung*), which depends either upon loss of tactile memories, or upon loss of memories associated with tactile memories (visual, olfactory, gustatory, etc.).

### (*g*) *Anomalies of Deep Sensibility*

Like the superficial senses the deep sensibility may be lost (*bathyanesthesia*), diminished, or, rarely, exaggerated. When lost or diminished we have to deal not merely with a loss of sensibility, but also with a loss of those unconscious centripetal impulses that play such an important part in the maintenance of muscle tonus, on the one hand, and of the coordination of muscular activities, on the other. Disturbances of these portions of the centripetally conducting neuron systems are, therefore, important factors in the origin of hypotony and of ataxia.

Exaggeration of the centripetal impulses here under discussion may result from irritation of any part of the peripheral centripetally conducting neurons (sensory neurons of the first order). An interesting example is seen in meningeal irritation, where, as a result of such exaggeration of centripetal impulses, marked hypertony appears (Kernig's sign).

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## 8. The Visceral Sensations and Their Anomalies

(*Centripetally Conducting Neurons of the Autonomic Systems*)

In examining the functions of the afferent neuron systems we should not lose sight of the autonomic groups.

The autonomic nervous system (Langley), formerly often referred to as the vegetative or visceral nervous system, consists of three main parts: (1) a mesencephalic part, (2) a bulbar part, and (3) a spinal or medullary part. The mesencephalic and bulbar parts include the portions of the N. oculomotorius, facialis, intermedius, glossopharyngeus and vagus that have to do with innervating structures not under the domain of the will (intrinsic muscles of the eye, the smooth muscles of the respiratory, circulatory and digestive systems, the salivary glands, sweat glands, lacrimal glands, etc.).

The spinal or medullary autonomic system includes the sympathetic nervous system proper, derived from the cervical, thoracic and lumbar portions of the cord, and the sacral autonomic system (domain of the N. erigens).

This autonomic nervous system contains both afferent and efferent neuron systems. The latter—probably by far the more important—will be dealt with further on. Here we have to consider only the afferent groups. These afferent autonomic neuron systems mediate visceral sensations due to the centripetal impulses of visceral origin (respiratory, circulatory, digestive, sexual), and also the subconscious or infraconscious centripetal impulses concerned in respiratory, vasomotor, secretory and digestive reflexes. This is a domain as yet very insufficiently investigated. In how far sensations of hunger and thirst, for instance, and the libido sexualis depend upon afferent impulses originating in the peripheral organs, and in how far upon chemical stimulation of nerve centers, has yet to be worked out. Neuralgic pains localized in the viscera probably pertain to this autonomic system. Very interesting in this connection is the conception of Head regarding the pains (so-called *referred pains*) and hyperesthesias in cutaneous areas due to visceral disease. Though the mechanism has not yet been fully worked out, I am of the opinion that the terminals or collaterals from afferent autonomic neuron systems end in arborizations upon the cell bodies of the peripheral sensory neurons in the spinal ganglia and influence the activities of the general peripheral sensory neurons. This influence is normally, as far as we know, so slight that we do not consciously recognize it, but in disease

there may be such an exaggerated stimulation from this source that hyperalgesia in cutaneous areas corresponding to the peripheral distribution of given spinal ganglia results. The determination of the existence of such cutaneous hyperalgesias is, therefore, of considerable importance in the recognition of visceral disease.

The afferent limbs of vasomotor and secretory reflex arcs deserve especial study, though relatively little work has as yet been done upon them. Notable, however, are the investigations upon the pressor and depressor nerves, branches of the N. vagus. Stimulation of the N. depressor causes a fall in blood pressure, probably through inhibition of the vasoconstrictor center in the medulla and dilatation of the blood vessels in the splanchnic area. A sudden increase of pressure in the aorta stimulates this N. depressor, obviously an important regulatory mechanism to safeguard the heart and arteries. The physiologists have worked out certain pressor reflexes leading to increase of blood pressure, as well as the depressor reflexes above mentiond.

Clinical methods of testing these vasomotor reflexes have not yet been adequately elaborated and the same is true of the secretory reflexes and those involving the muscles of the respiratory, digestive, and sexual tracts.

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## 9. The Senses of Taste and Their Anomalies

### (*a*) *The Four Taste Modalities*

There are four fundamental taste qualities—sweet, salt, bitter, and sour—mediated by special nerve endings in the tongue, and, probably, by special varieties of taste nerves.

### (b) *Tests for the Senses of Taste*

As stimuli, one uses substances in weak solution—sugar, common salt, quinin, tartaric or hydrochloric acid. It is well to have a chart divided into four squares (Fig. 525), each square marked with one of the four sense qualities, so that the patient may point to one of these squares when he experiences a sensation of taste without taking the tongue back into the mouth during the examination.

| | |
|---|---|
| Sweet. | Salt. |
| Bitter. | Sour. |

Fig. 525.—Chart to be Pointed at by the Patient When the Protruded Tongue Is Being Tested by Gustatory Stimuli.

One asks the patient to protrude the tongue as far as possible, gives him instructions how to respond, and then applies on the end of a glass rod a small drop of solution, using a separate glass rod for each fluid employed.

Each half of the tongue should be tested separately, and in each half the qualities recognized by the anterior two-thirds (N. lingualis) should

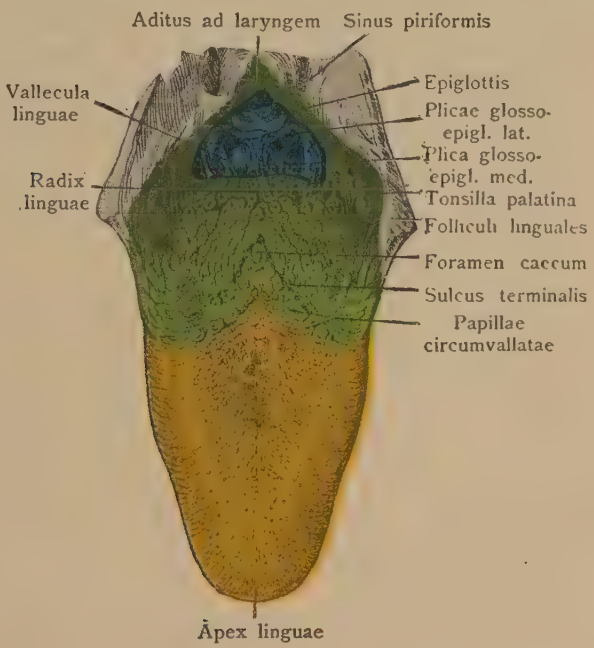


Fig. 526.—Distribution of the Nerves of Taste and Common Sensation in the Tongue. Green=N. glossopharyngeus; Blue=N. vagus (N. laryng-sup.); Yellow=N. trigeminus (N. lingualis). (After Corning in O. Veraguth, "Die klin. Untersuch. Nervenkranker," published by J. F. Bergmann, Wiesbaden.)

be noted as well as those recognized by the posterior third (N. glossopharyngeus), owing to the different nerve supply of these two parts.

The patient should be ignorant of the order of application of the test fluids, but it is well to apply the acid last, since it dulls the sensibility of all the organs of taste. Where difficulty is experienced in getting definite answers from the patient, and more than one set of tests is required, the mouth should be thoroughly washed out with water between the separate tests. The organs of taste respond also to electrical stimulation (galvanic taste) but electrical exploration is not needed for clinical work.

### (c) *Anomalies of the Senses of Taste*

As with the other senses, there may be an exaggeration, diminution or loss of function (*hypergeusia, hypogeusia* and *ageusia*). Occasionally there are perversions of taste (*parageusia*).

Sensations of taste experienced without local stimulation of the tongue are known as *gustatory hallucinations.*

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## 10. The Sense of Smell and its Anomalies

### (a) *Modalities and Methods of Testing*

One places narrow-necked vials containing various odoriferous substances in the nostril, asks the patient to sniff and to describe his sensations. Each nostril may be tested separately. There are a large number of smell modalities, but only a few of them need be tested clinically. It

will suffice to use oil of peppermint, oil of lemon, ether, tincture of asafetida, rubber, and cloves.

It should be kept in mind that normal people vary in their ability to discriminate among odors. Quantitative tests by Zwaardemaker's magazine-cylinder olfactometer are refinements that can scarcely as yet be clinically valued. Solutions of guaiacol (0.1 per cent), of ethyl bisulphid (0.01 per cent), of nitrobenzol (5 per cent) and of skatol (0.1 per cent), dissolved in liquid paraffin, are employed by Zwaardemaker.

### (*b*) *Anomalies of Olfactory Sense*

The anomalies of the sense of smell are expressed by the terms *hyperosmia, hyposmia, anosmia* and *parosmia,* similar to the terms used in describing anomalies of taste (*q. v.*).

In testing the senses of both taste and smell, it should be remembered that the mucous membranes carrying these sense organs are also supplied by nerves of touch, pain and temperature. Ammonia and formalin, for example, irritate the pain nerves of the nose (N. trigeminus). The so-called "tastes" of foods and drinks (aside from the qualities sweet, salt, bitter and sour) are in reality olfactory sensations resulting from vapors passing through the nasopharynx to the olfactory sense areas.

Mechanical obstructions in the nasal passages should be inquired into or ruled out before testing the sense of smell.

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## 11. The Sense of Hearing and its Anomalies

The sense of hearing may be roughly tested by the ordinary voice of conversation, or by ascertaining the distance from the ear at which the tick of a watch may be heard. When deafness exists, the external ear should be examined to make sure that it is not due to a plug of wax, and the condition of the middle ear should be tested (ear drum, ossicles, Eustachian tube).

### (*a*) *Auditory Acuity*

In more exact tests of the hearing capacity, one studies the grade of any disturbance present and tries to locate the seat of the disease. The distance at which the whispered voice can be heard is tested. Words like "measure," "say," "sex" can be heard, normally, further than words like "rue," "brood," "right," "row." Normally, in a quiet room, such whispered words should be heard at a distance of 20 to 25 meters. Should they not be audible at a distance of 6 meters, *auditory acuity* is certainly impaired. Each ear should be tested separately, and the patient should not look at the mouth of the examiner during the test. For still more exact examinations of auditory acuity, Politzer's acumeter may be used.

### (*b*) *Tone Perception*

In special cases it may be desirable to test tone perception. Otiatrists use the Bezold-Edelmann "continuous tone series," but one can get along very well by using six forks—C, c, $c^1$, $c^2$, $c^3$ and $c^4$ (Hartmann). Galton's whistle is useful for testing perception of the highest tones. Urbantschitsch's "harmonika" and Schultze's "monochord" are convenient instruments for tone testing. This testing of *upper and lower tone limits* is useful in distinguishing deafness due to middle ear disease from deafness due to labyrinthine or nerve disease. In diseases of the middle ear, it is especially the hearing of the lower tones that is involved, while in diseases of the cochlear nerve and the cochlea, the low tones may be well heard after the power to hear the higher tones has been lost.

When sensory aphasia (word deafness) is suspected, one should first make sure that the *tones* necessary for ordinary speech ($b^1$ to $g^2$) can be distinguished by the patient.

### (*c*) *Rinne's Test*

It is necessary also to make *Rinne's test.* The handle of a vibrating fork is placed upon the mastoid process behind the ear under examination and left there until it just ceases to be heard (bone-conduction); the vibrating fork is then held close to the opening of the corresponding ear, where, normally, it can still be heard for several seconds (air-conduction).

When the perception is, as normally, longer for air-conduction than for bone-conduction, the test is said to be positive (*Rinne* +); when the opposite is the case it is said to be negative (*Rinne* −). For this purpose one uses the fork C. Other tests, like those of Weber, Schwabach and Gellé, are of little importance in general medicine, though of interest to the otiatric specialist. A negative Rinne points to middle ear disease.

### (*d*) *Tuning-fork Tests of Bárány*

The ear of the patient and that of the examiner are connected by means of an air-tight rubber tube. To test air-conduction, the handle of the vibrating fork is placed on the rubber tube near the patient's ear; to test the bone-conduction it is placed on the patient's mastoid process. If the fork be placed on the ear-cartilage of the patient, the results should be the same as when placed on the rubber tube.

If the examiner's hearing and the patient's be normal, the sounds should be heard in each instance equally long, or perhaps a trifle longer by the patient. If the patient be deaf, the method permits of a differentiation between middle-ear disease and labyrinthine disease. In middle-ear disease, air-conduction and cartilege-conduction are shortened for the patient, while bone-conduction is not shortened. If bone-conduction is shortened for the patient, that is, if the examiner can hear the tone longer, the labyrinth or cochlear nerve is diseased. In pure disease of the internal ear, both cartilage-conduction and bone-conduction are shortened for the patient; if there be disease of both the middle ear and the internal ear, then the cartilage-conduction is shortened more than the bone-conduction. Thus the slightest participation of the internal ear becomes recognizable by Bárány's method.

### (*e*) *Test for Total Deafness in one Ear by the Noise-apparatus (Bárány)*

If one's hearing be normal, he may close both ears air-tight and still hear the ordinary conversational voice at a distance of several meters, and can hear the whispered voice close to the ear. Now if one hear normally in one ear, and be totally deaf in the other ear, the latter cannot be determined by ordinary methods since, even with the healthy ear closed air-tight, the conversational voice can be heard at least a meter away, and even a whisper close to the deaf ear may still be heard. Even the tests by the Lucae-Dennert method, and by the Bezold method are unsatisfactory. But by means of Bárány's "noise-apparatus" (*Lärmapparat*) entire certainty regarding unilateral deafness can be arrived at within a few seconds. By producing a sufficient noise, with this apparatus, in the healthy ear, this ear can be excluded entirely and the diseased ear can

then be tested by itself for its auditory acuity. Voss excludes the healthy ear by blowing compressed air into it.

### (*f*) *Galvanic Test for Cochlear Nerve (Volta-Brenner)*

If the cathode be placed in the external auditory canal and the anode in the hand of the patient, normally, as the current is strengthened, a sound is heard in the ear, first on cathodal closure of the current; on cathodal opening no sound is heard. If the anode be placed in the ear, a feeble sound is heard first on anodal opening, none on anodal closure.

In middle ear disease and in diseases of the internal ear, a feebler current than that normally required will give rise to the sound.

In certain cases a paradoxical reaction is obtained, the sound being heard in the ear opposite to that in which the electrode is placed. This is met with exclusively in instances of disease of the cochlear nerve (Friedrich).

### (*g*) *Test for Simulated Deafness (Bloch-Stenger)*

In medico-legal cases, a test to exclude simulated deafness is sometimes helpful.

If two tuning-forks, vibrating in unison, but one struck harder than the other, be held before the two ears of a person with normal hearing, the louder fork only will be heard. Let us suppose that a claimant asserts that he can hear nothing in his left ear. We now hold one fork, set feebly into vibration before the right ear; this the claimant hears. We next place the other fork, set strongly vibrating before the left ear (at the same distance), without removing the fork on the right. If the patient is really deaf or hard of hearing on the left, he will not experience any change in sensation. But if he, in reality, can hear normally on the left, the moment we place the fork before his left ear, the tone on his right will vanish, and the patient who simulates left-sided deafness will assert that he now hears nothing at all! Of course the simulation can be proved only when the simulant really has a normal ear on the side that he asserts is deaf.

### (*h*) *Anomalies of Sense of Hearing*

More general anomalies of the sense of hearing are included under the terms *hyperacousia, hypacousia* and *anacousia.* The so-called *hyperesthesia acoustica* does not necessarily indicate a refinement of the sense of hearing, but usually points to abnormal feeling-tones associated with auditory sensations due to an abnormally irritable cerebral cortex (functional neuroses). Other anomalies have been referred to under the several tests.

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## 12. The Sense of Sight and its Anomalies

The description of all the methods of examining the eyes belongs to the special branch of ophthalmology. Certain fundamental tests, however, must be made by the general practitioner and by the specialist in internal medicine. Every physician should be trained in the technic of the ophthalmoscope and of lenses, and should know the elementary methods of testing visual acuity and the state of the refractive apparatus, and of outlining the visual fields with the perimeter.

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### (a) *Testing for Dioptric Anomalies*

These are due either to (1) opacities of the refractive media (cornea, lens, vitreus) or (2) anomalies of refraction. In both, the image thrown on the retina is lacking more or less in sharpness. To detect these, it is well to follow a regular order of examination and the study of the media should always precede the examination of the eye-grounds, in order that false diagnoses may be avoided. In methodical sequence then, one proceeds as follows:

(i) Focal illumination of the cornea, anterior chamber, iris, pupil, and crystalline lens.

(ii) Anteroposterior illumination of the eyeball through the pupil.

(iii) Skiascopy or shadow test to determine the existence or non-existence of myopia.

(iv). In the non-myopic, distinguish between the emmetropic and the hyperopic eye.

After this preliminary study of the eye, we resort to ophthalmoscopy (1) with inverted image (2) with upright image, control of refractive anomalies; study of details of papilla N. optici, macula and periphery of retina.

#### i. Focal Lateral Illumination of Cornea, Anterior Chamber, Iris, Pupil and Lens

In a darkened room, the patient sits beside a light with a strong convex lens (15-20 diopters); the light of this lamp is focussed on the patient's eye. The surface of the cornea (curvature, smoothness) is first noted; opacities (old or recent keratitis) are systematically sought for. Next the depth of the anterior chamber is observed; one looks for inequalities of depth in each eye, also whether the depth is the same in the two eyes. The examination is important if swelling of the lens, subluxation of the lens, glaucoma, or iridocyclitis be suspected. In intraocular infections, there may be pus at the bottom of the anterior chamber (hypopyon).

In the iris, a search is made for signs of iritis (injected blood vessels), and the form, width and reaction of the pupils examined.

A preceding iritis causing adhesions between the iris and the lens (posterior synechiae) leaves a jagged pupillary margin; the irregularity will be exaggerated by a mydriatic (euphthalmin 0.5 per cent, or, if glaucoma be suspected, cocain 4 per cent). Sometimes an irregular pupil is due to partial paralysis (tabes, dementia paralytica), or, if oval, to glaucoma.

A radial slit (*coloboma*) may be due to a congenital anomaly, or to a preceding operation (iridectomy).

The *width of the pupil* varies much under normal conditions, but extreme dilatation (*mydriasis*) or extreme contraction (*myosis*) is usu-

ally pathological. One must be sure, of course, that no mydriatic (cocain, atropin euphthalmin, homatropin) or myotic (eserin) has been instilled into the eye before the examination! The internal administration of certain drugs must also be kept in mind (morphin contracts the pupils; belladonna preparations, hyoscin and scopolamin dilate them). I once had the chagrin of sending a patient to an ophthalmologist for a peculiar visual disturbance, having forgotten that I had prescribed, a few days earlier, belladonna suppositories for painful hemorrhoids! If mydriatics or myotics can be excluded, one next ascertains whether local inflammatory, traumatic or degenerative processes can account for a dilatation (*e. g.*, glaucoma, contusion) or for a contraction (*e. g.*, adhesions, atrophy of iris).

If the two pupils are unequal (*anisocoria*), the cause may lie either in a myosis of the smaller pupil (*e. g.*, paralysis of sympathetic) or in a mydriasis of the larger one (*e. g.*, sympathetic irritation or paralysis of autonomic innervation of the M. sphincter iridis).

The pupillary reactions (to light, to convergence) are next tested; the methods are described in the section dealing with the reflexes.

Finally, the condition of the lens is considered. If cataract exist, the pupil is widened; on focal lateral illumination radial gray stripes can be seen in the cortex of the lens, or a more diffuse central or pericentral opacity can be made out; on transillumination with a mirror, a cataract yields shadows, while if no cataract exist a clear red light is seen. If the lens be absent, the "candle-test" is conclusive. Normally, if a candle be moved back and forth in front of the eye in a darkened room, three images are visible: (1) An upright, small bright image on the anterior surface of the cornea; (2) a very small, inverted, clear-cut image on the concave posterior surface of the lens; (3) a larger, upright, feeble image on the convex anterior surface of the lens. On moving the candle, 1 and 3 move with the light, while 2 moves in the opposite direction. When the lens is absent (luxation, aphakia), images 2 and 3 do not appear.

### ii. Anteroposterior Illumination of the Eyeball through the Pupil

The patient sits in the darkened room with the lamp at one side of and a little behind his head. He is asked to look at the examiner's ear while light is thrown into the eye by means of the mirror of an ophthalmoscope. Normally the pupil then looks red. Opacities in the various media (lens, vitreus) will appear as shadows. As the examination proceeds, the patient is asked to look up, down and to each side; one notes whether the red reflex is everywhere clear. Thus opacities in the vitreus, cholesterin crystals, foreign bodies in the eye, or areas of detached retina (gray-green reflex) will come into view.

### iii. Skiascopy and Myopia

Anomalies of refraction are detected objectively by skiascopy (shadow-test). One determines whether or not short-sightedness (myopia), long-sightedness (hypermetropia, hyperopia) or normal-sightedness (emmetropia) exists.

The patient sits in the position described for anteroposterior illumination, *but a little more than a meter distant from the examiner,* and looks at a distant object, his accommodation-muscle having been previously put at rest by a drop of cocain solution (4 per cent) or one or two drops of homatropin solution (0.5 per cent).

Through the opening in a plane (not concave) ophthalmoscopic mirror, one observes the red pupil, and, rotating the mirror, allows the light to wander over the patient's eye noting how the red light in the pupil moves during the mirror-rotation. In the non-myopic eye the red light (with the shadow following it) moves in the same direction as that of the rotation of the mirror; in the myopic eye it moves in the opposite direction. If the eye be found to be myopic, the mirror is gradually brought nearer to the patient's eye, until the wandering of the red light in the opposite direction becomes indistinct; this is approximately the "far-point" of the myopic eye, and the distance is measured. A distance of 1 meter corresponds to a myopia of 1 diopter; a distance of 50 cm. indicates a myopia of 2 diopters.

### iv. Distinction between Emmetropia and a Hyperopia

If, on skiascopy, the eye be found to be non-myopic, the distinction between emmetropia and hyperopia is easily made.

The patient sits as in iii, but at a distance of 40–50 cm. from the examiner's plane ophthalmoscopic mirror. The light is thrown in slightly from the side in the direction of the papilla N. optici; the examiner, moving his own head slightly from side to side, notes whether or not distinctly-contoured retinal vessels are visible in the illuminated pupil. Myopia having been previously ruled out, if he now see these vessels distinctly, the patient's eye is hyperopic; if, on the contrary, only indistinct reddish striation is visible, the eye is emmetropic.

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### (*b*) *Ophthalmoscopy*

This can be used (i) for the control of refractive anomalies and (ii) for the study of the details of the eye-grounds.

#### i. Ophthalmoscopic Control of Refractive Anomalies

On examining with the ophthalmoscope for refractive anomalies, either the upright image or the inverted image may be used.

On using the *upright image,* the examiner's eye (corrected) and non-accommodating, held close to the non-accommodating eye of the patient, will see the details of the eye-grounds only when the rays coming therefrom are parallel (emmetropic eye). In hyperopia or myopia a convex or a concave lens must be turned in before the details become clear. The lens required gives the grade of hyperopia or myopia, if for the hyperopic eye we subtract the distance between the examiner and the patient from the focal distance of the convex lens, and for the myopic eye add the distance to the focal distance of the concave lens.

On using the *inverted image,* a convex lens of 10 diopters is held in front of the eye under examination. The emmetropic eye-ground will appear as an inverted image at a distance of 10 cm., the myopic eye-ground at a shorter distance, the hyperopic at a greater. Now if the lens itself be held at its focal distance (10 cm.) from the eye under examination, then every diopter of myopia will correspond to 1 cm. less, and every diopter of hyperopia to 1 cm. greater distance of this inverted image.

#### ii. Ophthalmoscopic Study of the Details of the Eye-grounds

Every medical student should, during his medical course, become thoroughly familiar with the use of the ophthalmoscope (direct and indirect ophthalmoscopy). The technic is not difficult, and the information obtainable by ophthalmoscopy is so important that unacquaintance with the methods and failure to apply them are no longer excusable in a medical practitioner. The *electrical ophthalmoscope,* with storage battery in the handle, so compact as to go easily in one's consultation bag, is now an indispensable part of the practitioner's instrumentarium. The convenience of this instrument has resulted in the commoner use of direct ophthalmoscopy with upright image; it has the advantage also of greater magnification of details. The examination by the indirect method has the advantage of revealing a much larger field.

##### (*1*) *Indirect Ophthalmoscopy* (*Inverted Image*)

The patient sits within reach of the examiner in a darkened room, with the source of light behind and to one side of his head, and looks to-

ward the wall past the side of the examiner's head at the level of the examiner's eye; in this way, the examiner is enabled to look into the patient's eye, a little from the side, in direct line for the papilla N. optici. After throwing the light into the patient's eye from the mirror of the ophthalmoscope, and finding the region of the papilla (recognizable by the lighter color of the reflex), a convex lens (15 diopters), with handle, held between the finger and thumb of the left hand is brought in from the side and above and placed about 8 cm. in front of the patient's eye, the spread fingers supporting themselves on the patient's forehead. Care must be taken by the examiner not to cover the opposite eye of the patient at any time by the hand holding the lens, since it is with this eye that the patient fixes, in order that both eyes may be held steady. If the inverted image of the papilla does not become visible at once, it is best to begin all over again and make sure that (1) the patient is looking in exactly the right direction, (2) the lens is held in precise position, and (3) the distance between examiner and patient is sufficient. Many find it easier to turn in a convex lens of 2 to 4 diopters behind the opening in the ophthalmoscope; if the examiner is himself myopic, this convex glass will not help him. The examination is facilitated by the use of a mydriatic (euphthalmin, homatropin, cocain). If glaucoma be suspected, great caution should be used in producing mydriasis.

### (2) *Direct Ophthalmoscopy (Upright Image)*

This is somewhat difficult with the old-fashioned ophthalmoscope which was not self-illuminating but is so easy with the modern electric ophthalmoscope, and can be so conveniently used on a patient lying in bed that the tyro need have no difficulty with it. Indeed, it seems likely now that direct ophthalmoscopy will largely replace the indirect method, at any rate, among general practitioners. The electric light is turned on by the switch in the handle of the instrument, which is then brought close to the patient's eye, the latter being so directed that the papilla N. optici (with its vessels) comes at once into view. Even when a patient is unconscious it may be possible to get a good view of the eye-grounds by this method! If necessary, a convex, or concave, lens may be turned in, to make the details of the eye-ground clear.

### (3) *The Normal Eye-ground*

The papilla N. optici is normally sharply circumscribed, its edges being everywhere sharply marked off from the surrounding retina. It is of a delicate rose-color, the temporal half being a little lighter in color than the nasal half. The physiological excavation (or optic cup) looks white; it varies in size and depth; it may be central or excentric, but it rarely involves the whole papilla, and the papilla in its periphery is rose-

colored. The blood vessels extend from the center of the papilla upward and downward, branching dichotomously. The paler, narrower arteries are easily distinguishable from the veins. With a little experience one comes to recognize deviations from normal color, width and fullness.

To bring the macula lutea into view, the patient looks directly forward into the ophthalmoscope. The region of the macula lutea is devoid of blood vessels, is a little darker in color than the rest of the retina; in the center it is of a slightly brownish-red tint. When the seat of pathological change (vascularity, light or dark spots, cherry-red spot inside a bluish-white area in amaurotic idiocy), it is easier to see than under normal conditions.

The general retina peripheral to the papilla owes its red color to the vascularity of the tunica choroidea. Ordinarily it looks evenly red or brownish-red, being a little darker in brunettes and in negroes than in blondes. In very blond persons, most markedly in albinos, the blood vessel anastomoses in the choroid may be visible with pale intervascular spaces. In darker people with more pigment, these intervascular spaces may appear as gray areas, giving the eye-ground a mottled or checkered appearance, always easily distinguishable, however, from the pathological pigmentations met with in retinitis pigmentosa and in chorioiditis disseminata.

### (4) *Pathological Eye-grounds*

Only the more important and easily recognizable alterations can be referred to here. For more details, special texts may be consulted.

**I. Changes in the Papilla N. optici.**

(1) Optic Neuritis (*Neuritis optica*).—The disk looks grayish red and opaque; its margins are indistinct; the blood vessels, especially the veins, are dilated and tortuous (hyperemic). In the papilla itself, or in the adjacent retina, minute hemorrhages or radially-arranged, grayish-white spots or bands may be visible. The change may be unilateral or bilateral. When the disc is greatly swollen (2 diopters or more) and the papilla increased in diameter, the condition is known as *choked disk,* and points to increased intracranial pressure. Should this pressure diminish and the choked disk recede, it is followed by secondary optic atrophy (neuritic atrophy), the disc growing whiter, its margins remaining, however, indistinct (distinction from primary optic atrophy), the blood vessels remaining tortuous, or becoming narrowed and ensheathed, the adjacent retina undergoing pigmentary change.

In "retrobulbar neuritis," the changes above described do not appear; the papilla may long remain unaltered, though after a time it may show a pallor, more marked on the temporal side, due to a slow retrograde

atrophy of the fibers of the optic nerve. This retrobulbar neuritis may be acute (*e. g.*, in rheumatic fever, in multiple sclerosis), or chronic (*e. g.*, in toxic amblyopias due to tobacco, alcohol, wood alcohol, etc., and in diabetes mellitus).

(2) Optic Atrophy (*Atrophia N. optici*).—The papilla loses its rose color and looks white, grayish-white, or greenish-white.

(a) *Simple Atrophy* (*"Primary Optic Atrophy"*) such as that seen in tabes and in dementia paralytica. The disk turns pale, but its margins remain distinct and sharp, and there are no marked changes in the vessels. The pallor of the disk becomes visible as soon as the patient complains of the visual disturbance, thus differing from the simple atrophy following "retrobulbar" neuritis in which the visual disturbance always exists for a considerable period before the pallor of the disk becomes noticeable.

Following embolism or thrombosis of the central artery of the retina, after the acute signs have passed off, a simple optic atrophy develops, but it is characterized by the accompanying extreme contraction of the vessels.

(b) *Neuritic Atrophy* (*"Secondary" Optic Atrophy*).—This follows optic neuritis, and has been described above in connection therewith.

(c) *Optic Atrophy in Retinal Disease.*—In degenerative processes involving the retina diffusely (*e. g.*, chorioretinitis, retinitis pigmentosa) the papilla turns yellowish-white and opaque; the blood-vessels are narrowed; the retinal degeneration is obvious.

(d) *Glaucomatous Optic Atrophy.*—In chronic glaucoma, owing to the long continued high intra-ocular pressure, "glaucomatous excavation" occurs, involving not only the whole disc but also some of the retina peripheral to the disk. The abrupt bending of the blood vessels at the edge of the papilla is a striking feature.

**II. Changes in the Retina.**

(1) Acute Retinitis or Neuroretinitis.—The retina looks turbid, and shows hemorrhages and grayish-white or white spots or stripes.

(a) *Retinitis albuminurica.*—White spots in the retina; in the region of the macula, stellate white lines ("splash"), usually associated with retinal hemorrhages and turbidity of the papilla, appear.

(b) *Retinitis diabetica.*—Irregular white spotting and stippling with hemorrhages but without the macular "splash" and without papillary turbidity.

(c) *Retinitis anemica.*—Extensive hemorrhages, small arteries, tortuous veins of lighter color than normal, opacity of papilla. White spots and bands may or may not be present, but are not a prominent

feature. This change is seen in some cases of pernicious anemia, scurvy, purpura, etc.

(d) *Retinitis leukemica.*—In myelogenous leukemia, the eye-ground looks pale yellow, the veins tortuous but pale yellow in color. The retina may also show changes as in (c).

(e) *Retinitis septica.*—Round white spots and hemorrhages near the papilla, the latter looking normal or only slightly hyperemic.

(2) Chronic Retinitis and Retinal Atrophy.

(a) *Retinal Atrophy after Luetic Chorioretinitis, etc.*—Narrowing of retinal blood vessels; degeneration of papilla; black pigment deposits.

(b) *Retinitis pigmentosa.*—Changes similar to *a* may occur, independent of preceding inflammation; often hereditary.

(c) *Amaurotic Family Idiocy* (Sachs).—In macular region, a cherry-red spot, surrounded by a bluish-white area; optic atrophy.

(3) Detached Retina.—This is best seen by throwing the light directly into the eye (upright image) and looking for a gray or gray-green color; the folds of the retina may resemble a comb; the dark blood vessels are tortuous; they follow the folds.

(4) Tumor of Retina (*Glioma, Sarcoma*).—Usually the pupil is wide and, with the naked eye, a yellow "reflex" becomes visible behind the lens. This has been called the "amaurotic cat's eye."

### III. Changes in the Choroid.

The two changes most important for the internist are disseminated choroiditis and miliary tuberculosis.

(1) Choroiditis disseminata.—If acute, one sees vaguely delimited gray or grayish-yellow round spots, often crossed by retinal blood vessels. As these grow older, they become atrophic, the sclera shows through, and whitish areas, sharply delimited, with pigment at their borders or within them, appear. Retinal vessels and papilla unaltered.

(2) Miliary Tuberculosis.—Changes like those of choroiditis disseminata in the acute stage.

(3) Staphyloma posticum or Conus-formation in Myopia.—In high-grade myopia, a tension-atrophy of the choroid may occur at the papilla and in the retina on its temporal side (*staphyloma posticum*). The macula may be involved. The white color of the sclera shows through.

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### (c) *Functional Tests of Vision*

These include (i) the tests for visual acuity; (ii) the tests for color vision; (iii) the delimitation of the visual fields (perimetry); (iv) the tests for night-blindness (hemeralopia), and (v) the tests for simulated visual disturbance. The tests for the eye-muscles are described in the section on disturbances of motility.

#### i. Testing the Visual Acuity

In order to see perfectly (1) the refractive media of the eye must not hinder the passage of light; (2) the pupil must make a proper diaphragm or blend; (3) the light rays must be properly focused as a sharp inverted image on the retina; (4) the neurons of the optic conduction path from the retina to the cortex must not be injured, and (5) the cortical visual center, the association centers, and the paths connecting them must be intact.

When an opacity of the lens (cataract) is present, one cannot of course apply the reading test, but one may draw conclusions regarding the integrity of the visual sensory conducting path by holding a candle at a distance of six feet from the eye and, alternately illuminating and shading the eye, the patient being asked to say whether he has any light sensation or not.

For roughly testing vision, one places the patient with his back to the window, and, making movements of the hand or fingers before him, asks him to describe what he sees, to count the number of fingers outstretched, or to imitate with his own hands and fingers what he sees. The exact distance at which the fingers can be recognized is measured.

For finer tests of visual acuity one uses Snellen's or similar test types.

Each letter or figure is as broad as it is long; the strokes of the letters are of even thickness, one-fifth the width of the whole letter. It is desirable to have an illumination of constant strength, such as is afforded by Roth's apparatus. One must have also a double series of concave, convex and cylindrical lenses; also a set of prisms and some smoked glasses; a red glass, a milky glass or a metal disk for closing one eye; and lens holders, preferably the "universal aluminum holders" of Sydow. The visual acuity V (*visus*) is expressed by a fraction; the numerator gives the distance $d$ in which the letter is recognized, the denominator is the distance $D$ that corresponds to a visual angle of five minutes for the letter: $V = \frac{d}{D}$.

If the eye examined shows, without lenses, a normal or supra-normal visual acuity for the test types at a distance ($\frac{20}{20}$ or more) it is either emmetropic or hypermetropic (self-corrected by contraction of the accommodative muscle). If it be hypermetropic, it will still retain its best vision with convex lenses (relaxation of accommodation). The strongest convex lens with which the best vision is retained gives the degree of hyperopia existing.

If the eye does not possess normal acuity of vision for objects at a distance, the fault may be (1) a refractive anomaly (corrigible by lenses); (2) an organic or a functional disease of the retina or of the visual paths; (3) simulation; or (4) combinations of the foregoing.

*Hypermetropias* can be corrected by convex lenses, *myopias* by concave lenses (the weakest concave lens that gives maximal visual acuity determines the degree of myopia existing) and *astigmatic anomalies* by lenses that correct certain meridians. The astigmatism with stronger refraction in the horizontal meridian is known as "astigmatism against the rule." The diagnosis is made with the aid of Green's "star-figure."

Defective visual acuity not due to refractive errors, as that existing after correction of the latter by glasses, may be slight (*amblyopia*), or there may be complete blindness (*amaurosis*). It should never be forgotten that diseases of the visual paths may coexist with refractive anomalies.

*Sudden blindness of one eye* may be due to embolism or thrombosis, occasionally to spasm, of the central artery of the retina. Other causes of sudden disturbances of vision include (1) vascular lesions of the cerebrum, (2) retinal detachment, and (3) choked disc. Fairly sudden visual injury may follow (1) acute glaucoma, (2) hemorrhages into the vitreus, or (3) acute retrobulbar neuritis.

The determination of *accommodative power* (testing for *near vision*) will be described under the testing of the M. sphincter iridis and M. ciliaris (see Efferent Autonomic Neuron Systems), where the different forms of *asthenopia* are taken up.

### ii. Tests for Color Vision (Determinination of the Type of Central Vision)

Normal vision is *trichromatic,* or, better, *polychromatic;* the person can see the spectrum in its natural colors (normal polychromatic vision of Kirschmann). The commonest form of color-blindness is that in which many colors are seen, but the vision differs from the normal in that (a) one or more color-qualities are absent, or (b) certain colors resemble one another more closely than normal, red or green often being confused with other colors (so-called abnormal polychromatic vision of Kirschmann). In *dichromatic vision* (so-called red-green-blind), the partially color-blind people see only two colors in the spectrum, yellow on the one side and blue on the other. Between the yellow and the blue is a narrow colorless domain where normal people see blue-green. The most useful colors for testing are (1) rose (bluish-red), (2) gray, (3) bluish-green. To the ordinary patient, suffering from partial color-blindness, red, orange, yellow and yellowish-green are all seen, when equally illuminated, as shades of yellow, while violet, indigo, blue are all seen as shades of blue. For some of these patients the red end of the spectrum is shortened, and the brightest spot in the spectrum for them lies to the right of the sodium line (so-called *red-blind* people or *protonopes*); where the spectrum is of normal breadth toward the red, we speak of the so-called *green-blind* people or *deuteronopes.*

The totally color-blind, or achromates of Kirschmann, confuse all colors, as they can recognize only differences in brightness, all lights yielding sensations of gray in varying intensity. For them, the spectrum is colorless and considerably shortened toward the red end, the brightest spot in the spectrum lying where normal people see the bluish-green. Most of these patients have diminished central vision, photophobia and nystagmus.

For practically testing the color vision, in general, one uses (a) Holmgren's colored wools or (b) Stilling's pseudo-isochromatic charts.

**Holmgren's Colored Wools.**—A large collection of different colored wools are placed before the patient. The examiner selects a rose-colored sample (pale bluish-red), and asks the patient to place beside it all those that have the same color, no matter whether they look brighter or darker to him. He should be told that mistakes consist either in placing wools of the wrong color with the sample or of leaving wools of the same color behind. The partially color-blind will place bluish-green and gray wools with the rose-colored sample. The test may be carried further by selecting a bluish-green or a gray wool as the sample.

The totally color-blind (achromates) will see no differences among the samples, except variations in brightness.

**Stilling's Charts.**—These charts contain a mosaic of colored areas in which one can at will place one of the colors likely to be named wrong

by the partially color-blind. The patient may be wholly unable to recognize any difference between the color inserted and the general color of the chart.

### iii. Delimitation of the Visual Fields (Perimetry)

A preliminary rough test may be made as follows: Close one eye by means of a light bandage; let the patient sit with his back to the window and in such a position that the test-object will be well illuminated. The examiner's clothes should be of a dark color. Ask the patient to look directly into the eye of the examiner opposite him, 40 cm. distant. Now bring the test-object midway between examiner and patient, when the examiner's visual field may be used as a control for that of the patient. If the patient's visual field differ markedly in extent from that of the examiner, an exact determination by means of the perimeter should be undertaken. With this preliminary rough test, the experienced clinician can usually detect a hemianopsia, a scotoma, or a concentric contraction of the fields, if present. Perimetry is indispensable for exact neurological work.

**Perimetric Examination.**—The simpler perimeters do very well. Self-registering perimeters, though convenient, are not necessary for ordinary clinical work. The patient's chin rests on the support, his back to a window, his eyes on a level with the middle of the perimeter, and he is told to look straight forward with the unbandaged eye and on no account to look to one side, or to follow the object with his eye, though he is permitted to wink.

The attention of the patient must be concentrated on the test and the test-object (1 cm. square), then white, may be brought gradually into the visual field with a vibrating movement, the patient being asked to state when he first perceives the movement of a light spot. After the field for white has been delimited, the color-fields may be examined. Colored objects should not be brought in vibrating, but the patient should be told to watch closely and to state the moment when he has an impression of color and to name the color. He may see a light spot before he sees a color, but should wait until a definite color-impression that he can name is perceived before he responds.

The colors should be changed frequently. No attempt should be made to outline the whole visual field for a single color at once. The patient is not permitted to know what color is about to enter the visual field.

In general one passes from the outside in, rather than in the opposite direction, when testing the periphery of the visual field. Defects within the field itself (so-called *scotomata*) are similarly outlined, the test-object being passed out of the scotomic areas into the areas that can be seen. When a scotoma is small, a test-object measuring 3 mm. in diameter may be used to delimit it. If there be a central scotoma, then the patient

should fix his eye not on the center of the perimeter, but on some marked eccentric point (so arranged that on looking at it, the middle of his cornea is opposite the middle of the perimeter).

The perimeter must permit of exact reading in degrees. The test-object is brought along the several meridians until it is seen. The

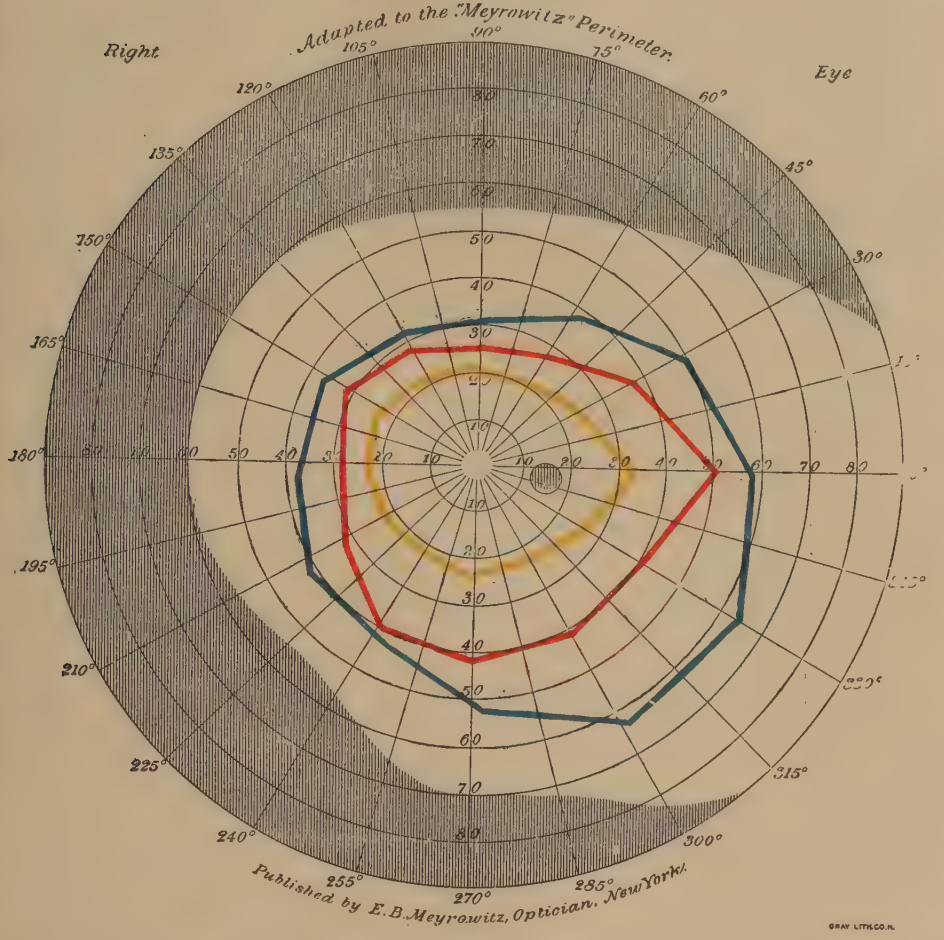


Fig. 527.—Visual Fields as Outlined on Perimetric Chart. The Normal Fields for Color Vision Are Also Shown.

results are charted at once in the blank schemata devised for the purpose. Deviations from the normal are thus at once recognized.

In testing colors, blue, red and green will usually be sufficient. It is to be remembered that the visual field for white light is much greater than that for colors and that the fields for the several colors differ from one another; in other words, the periphery of the visual field is, normally,

totally color-blind (achromatic). Then follows a zone in which only blue and yellow can be seen (dichromatic). In the middle portions all colors become visible (trichromatic or polychromatic). Red can usually be seen in a larger visual field than green with the test-object ordinarily used (cf. Fig. 527), though, if a green that is complementary for red be employed, the fields for red and green are approximately co-extensive.

**Defects Encountered.**—Great care should be taken in valuing perimetric examinations. Patients of low intelligence, or those that have difficulty in concentrating the attention, or who become quickly fatigued, may yield very different results on different occasions. Defect of one-half of a visual field is known as *hemianopsia.* This may be unilateral, but is usually bilateral. When the two right halves or the two left halves of the field are lost, *i. e.,* if the nasal half on one side and the temporal half of the visual field on the other are simultaneously involved, we speak of bilateral homonymous hemianopsia (*hemianopsia homonyma*), but if the right half of the visual field be affected on the one side and the left half on the other (either the two nasal halves or the two temporal halves simultaneously) we speak of heteronomous hemianopsia (*hemianopsia heteronyma*). If both temporal fields be affected (as in chiasm lesions), it is a bitemporal hemianopsia. Binasal hemianopsia is exceedingly rare. Of course, bilateral hemianopsia depends upon bilateral retinal hemiblindness or hemiopia; thus, when the right halves of both visual fields are defective, it is the left halves of the retina of the two eyes that are blind.

If in a hemi-anopsia, it is the color-sense that is chiefly involved, we call it a *hemi-chromatopsia;* if vision be present but dim, we speak of *hemi-amblyopia.*

In *total hemi-anopsia* the line separating the blind from the non-blind area passes perpendicularly through the fixation point; in a hemianopsia that is not total, the blind-half is encroached upon by an area of visibility—the so-called *surplus field.* If this surplus field be so large that only a quadrant of the total field is invisible we speak of a *quadrantic hemianopsia.* Smaller defects in the field are called *scotomata;* normally there is a scotoma, corresponding to the blind spot of the eye (optic disc). A *central scotoma* is one at, or near, the fixation-point; it may involve only the red and green as in the retrobulbar neuritis limited to the papillomacular bundle often met with in nicotin poisoning and in alcoholism, and it is then spoken of as a *relative scotoma,* but if no light at all be perceived, as in some cases of diabetes or of multiple sclerosis, it is an *absolute scotoma.*

By *concentric contraction of the visual fields* is meant a general restriction at the periphery. In primary and secondary optic atrophy, such a contraction, as it develops, proceeds from the periphery centralward, though the central acuity both for white and colors may also suffer early.

The "foggy" vision comes on slowly in tabes and in dementia paralytica, but may appear suddenly in the optic neuritis due to lues or to meningitis. In *choked disk*, due to brain tumor, lues, hydrocephalus or brain abscess, the vision may remain good for a time, but if the intracranial pressure be not lowered (say by decompression or by antiluetic treatment) secondary optic atrophy will develop, and the visual fields will undergo contraction, the color-fields sometimes being involved first (Bordley and Cushing).

In glaucoma, the medial field is first involved; an eccentric temporal area may be long retained, the so-called *glaucomatous visual-field slit.*

A so-called *ring-scotoma* is occasionally encountered, especially in retinal atrophy due to luetic chorioretinitis or to retinitis pigmentosa. It is due to the localization of the degenerative process in an intermediary zone of the retina, later extending both toward the center and toward the periphery.

Sometimes the visual fields are so contracted that only an "island" of central vision remains in each eye; it is as though the patient were looking through a small tube. This condition may be due to serious retinal atrophy, but it is often met with in the functional neuroses (hysteria, traumatic neurosis).

The above-mentioned defects are all *immobile positive scotomata;* the movable shadows due to opacities in the vitreus are called *mobile positive scotomata.* The opacities may be visible with the ophthalmoscope; in neurasthenia and in myopia certain *muscae volitantes* in the form of threads, flocculi or chains may be complained of when the vitreus is normal (*myodesopsia*). In migraine, an attack may be ushered in by the so-called *fortification scotoma*—a jagged glimmering, followed by a darkening.

### iv. Test for Night-blindness (Hemeralopia)

Darken the room, and note whether the patient can see as long as the normal examiner and can as quickly adapt himself to changes in intensity of illumination. Exact determinations may, if desired, be made by Foerster's photometer.

When the patient can see better in dim light than in bright light, he has *nyctalopia;* this is met with in beginning cataract, as the dilatation of the pupil in the dim light uncovers more of the transparent part of the lens.

If a patient cannot see in dim light, or only after long adaptation, he has *hemeralopia* or night-blindness. This may be due to retinitis pigmentosa, especially if it occur in childhood. Sometimes it is met with in glaucoma, in diffuse choroiditis and in retinal detachment. It may occur, temporarily, in states of exhaustion or intoxication (malnutrition, or cachexias).

### v. Tests for Simulated Visual Disturbance

If simulation be suspected, one should make the tests for it before revealing the suspicion to the person under examination.

The conditions most often simulated are (a) blindness in one eye (unilateral amaurosis) and (b) feeble vision in one eye (unilateral amblyopia).

(a) **Simulated Unilateral Amaurosis.**—One uses tests that the patient believes do not involve the use of the eye that he asserts is blind.

(1) The Double Image Test (Graefe).—Cover the eye said to be blind. In front of the other, place a prism (base above or below) so that its edge goes exactly through the middle of the pupil; this causes monocular diplopia. Next, surreptitiously uncover the covered eye and simultaneously shove the prism entirely over the pupil of the "healthy" eye. If the patient continues to see double—the simulant usually asserts that he does—he must see with both eyes to do so.

(2) The Reading Test.—Place a lens-holder on the nose of the patient. In front of the eye said to be blind, place a plane glass (or if there be a refraction error, a glass correcting this). Then in front of the "healthy" eye, place a strong convex glass, which will make clear vision at a distance impossible for this eye. If the patient can read any of the test-types, he is "caught."

(b) **Simulated Unilateral Amblyopia.**—The reading test above mentioned will usually suffice. If not, the mirror test (see special texts) may serve to detect the simulation.

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## 13. The Vestibular Senses and Their Anomalies

In recent years, we have come clinically to value the great group of centripetal impulses that reach the brain through the vestibular nerve (*N. vestibuli*). The information that the brain receives regarding the position of the head when it is at rest, and regarding the acceleration or retardation of progressive (non-rotary) movements, seems to depend upon impulses arising from the stimulation of the nerve-endings in the utricle and saccule, upon which the little ear-stones (otoconia) rest. Every normal person recognizes the direction "up" and "down," even when under water; the same mechanism is sensitive to accelerations in a straight line.

The information that the brain receives regarding angular accelerations, or the change of velocity of rotary movements, seems to depend on impulses arising from stimulations of the nerve-endings in the ampullary crests of the membranous ampullae of the semi-circular ducts.

Alterations in the position of the head relative to the vertical causes a compensatory change in the setting of the eyeballs; rotation of the body around its vertical axis causes nystagmus. The eye-muscle reflexes of vestibular origin have come to assume an important rôle in clinical diagnosis.

It is interesting that in deaf-mutes, there is often loss of orientation as to the vertical when under water and also often absence of vertigo in rotation, probably due to vestibular lesions.

### (*a*) *Clinical Testing of the Functions of the Vestibular Apparatus*

During the past decade, thanks especially to the researches of R. Bárány, we have been supplied with a series of tests for the vestibular functions, of great importance for differential neurological diagnosis. In America, the tests are gradually becoming adopted. My attention was first directed to them by Dr. S. J. Crowe. In the following section, I have drawn largely upon the several publications of Bárány, and especially upon the account given by him in Lewandowsky's *Handbuch*.

A thorough testing of the vestibular apparatus requires (according to Bárány) the examination of the following:

I. Spontaneous nystagmus.
   (a) By deflection of the eyes to the side.
   (b) Behind opaque spectacles.

II. Nystagmus caused by quick movements of the head. (Position in bed; abnormal attitude of head).
III. Caloric nystagmus.
IV. Nystagmus on rotation of the body.
V. Galvanic nystagmus.
VI. Nystagmus, or vestibular eye-movements, caused by increasing or reducing the pressure of the air in the external auditory canal.
VII. Vestibular disturbances of equilibrium.
(a) Spontaneous disturbances of equilibrium.
1. Are they related to an existing nystagmus?
2. Is the direction of falling influenced by rotation of the head?
(b) Experimental vestibular disturbances of equilibrium (reaction-movements) due to irrigation, rotation or galvanization; relations of these to nystagmus and to head-attitude; influence on spontaneous disturbances of equilibrium.
VIII. Tests for vestibular reaction-movements in the extremities. (Pointing with eyes closed to objects previously seen or touched.)
IX. Anamnestic vestibular data. Statements of the patient regarding sham-movements of external objects, sham-rotation of his own body, nausea, vomiting, pallor, sweating, tremor and decreased or increased susceptibility to vertigo.
X. Examination of the rotation of the eyes opposite to lateral flexion of the head.
XI. Examination of the vestibular eye-movements in cases of eye-muscle paralysis, or of conjugate deviation.
XII. Examination for optic nystagmus.

These methods will be considered *seriatim* but, of necessity, in great brevity. They are too important to be omitted; those desiring a more detailed account should consult the original publications of Bárány.

### i. Spontaneous Nystagmus

Vestibular nystagmus is composed (1) of a slow, and (2) of a quick movement. It is the slow movement, solely, that is due to the vestibular apparatus; the quick movement is central (supranuclear) in origin. Custom has established that the direction of the nystagmus shall be named according to the direction of the quick movement.

In form, a vestibular nystagmus may be horizontal, rotary, vertical, diagonal or a combination of these. The direction of the rotary form is named after the direction of the quick movement of the upper end of the vertical meridian of the iris. Looking in the direction of the quick move-

ment intensifies a vestibular nystagmus, while looking in the direction of the slow movement lessens or stops it.

To test for spontaneous nystagmus, the patient is asked to look at the finger of the examiner at a distance of about one meter. On strong lateral deviation of the eyes, about 60 per cent of normal persons show a minimal horizontal and rotary nystagmus, which is, clinically, of no importance. The higher grades of horizontal and rotary nystagmus on lateral deviations, other forms of spontaneous nystagmus, and every nystagmus, however slight, appearing on looking straight forward, must be regarded as pathological.

If no nystagmus appear on looking straight forward, place opaque spectacles in front of the eyes similarly directed; a nystagmus will sometimes appear, and if so, it is pathological.

The nystagmus due to disease of the peripheral vestibular nerve or end-organ is always a combination of horizontal and rotary nystagmus in the same direction; every other form of spontaneous nystagmus has an intracranial origin.

But a nystagmus of intracranial origin may also be both horizontal and rotary; the form alone is, therefore, not decisive, and one must be guided by functional tests and by longer observation of the nystagmus. If, for example, the nystagmus be both horizontal and rotary to the right, it could have a peripheral origin in the vestibular apparatus of the right side only when this end-organ is still capable of functioning; should now the functional test show that this apparatus on the right is unexcitable, the proof would be brought that the nystagmus has an intracranial origin. Should, however, the local apparatus on the right be found to be excitable, the only way to decide between a peripheral and an intracranial origin is to observe it during several days; should it continue in undiminished intensity longer than 24 hours, it is intracranial in origin. If it last less than 24 hours, or if it alternate with nystagmus in the opposite direction, or if nystagmus-free intervals occur, it may be either of peripheral or intracranial origin. The decision will then have to be based on the other symptoms in the case.

If, on the contrary, there be horizontal and rotary nystagmus toward the healthy side, it may be due to an acute destruction of the end-organ, or to a sudden lesion of the N. vestibuli before its entrance into the medulla oblongata. In either case, it must decrease in intensity daily and by the end of a fortnight be reduced to a very slight excursion. Should it turn out, on close observation, that there is no definite reduction of intensity at the end of several days, it must have an intracranial origin.

### ii. Nystagmus Caused by Quick Movements of the Head

If the head of a normal person be bent quickly back, to one side, or forward, or if it be rotated to right or left, nystagmus occurs during the

movement, but at the end of the movement the eyes remain at rest (aside from the "opposite rotation" to be described under Caption x).

In *partial* injuries of the vestibule or of the N. vestibuli, definite attacks of nystagmus are set up during the quick movement of the head, and last from 10 to 30 seconds. The form of the nystagmus varies with the way the head is moved. The attacks are most marked and most constant on bending the head quickly toward the side of the vestibular lesion. Such patients have attacks of dizziness on quick movement of the head (Bruns). After one attack has been elicited, movements may be made for some time without another occurring, except in lesions about the 4th ventricle.

On lying in bed, turning to the left or to the right side may call forth an attack. The attitude of the patient in bed, and on sitting, should be noted.

### iii. Caloric Nystagmus

If one irrigate for about 20 seconds the right ear (the head upright) of a normal person with water at a temperature below that of the body, a horizontal and a rotary nystagmus toward the left will appear, and will last for about two minutes. If water warmer than the body be used, a rotary nystagmus toward the right will appear.

It matters not whether the ear drum be perforated, though if the perforation be dry, air may be blown in instead of irrigating with water. The external auditory canal should be cleansed before making the test. A temperature of 25°–30° C. is best for the cool test, and one of 45°–48° C. for the warm irrigation.

The eyes should be watched closely, so that the irrigation may be stopped the moment distinct nystagmus begins; in this way violent vertigo, nausea and vomiting can be avoided.

If a patient be unconscious, cold irrigation causes deviation to the irrigated side instead of nystagmus.

When spontaneous nystagmus exists, the test is difficult. If, for example, there be a rotary nystagmus to the right and to the left, cold irrigation of the right ear will lessen or stop the nystagmus to the right and intensify the nystagmus to the left.

If one labyrinth be destroyed (suppuration, hemorrhage, lues), or if the N. vestibuli be injured (neuritis, compression) cold irrigation of the ear on the same side will elicit no reaction; the reaction on the other side may be normal, though often it is less than normal, and may be absent.

A lessened or an increased caloric reaction is harder to judge of than an absence of reaction. Efforts are being made to work out graphic methods of registration that will permit of quantitative judgments. Lessened reaction occurs in partial lesions. Increased excitability has been met with in brain tumors.

### iv. Nystagmus on Rotation of the Body

Rotation of the body stimulates both labyrinths simultaneously. If the body be turned to the right in a rotating chair, evenly, about 10 turns in 20 seconds, and then be suddenly stopped, a horizontal nystagmus to the left will appear and will last about 42 seconds.

Clinically this test need be but little used, though it is helpful in detecting simulation in cases of trauma followed by alleged vertigo (Bárány).

### v. Galvanic Nystagmus

One electrode is placed in front of the tragus or in the external auditory canal of the ear to be examined, the other at an indifferent site (forearm, neck, chest, forehead).

If the cathode be in the right ear, closure of the circuit elicits rotary nystagmus toward the right; if the anode be in the same ear, the rotary nystagmus is toward the left.

Destruction of the labyrinth does not abolish galvanic nystagmus; lesion of the N. vestibuli does abolish or diminish it.

### vi. Effects of Compression or Rarefaction of Air in the External Auditory Canal

In normal persons, nystagmus or vestibular eye-movements cannot be elicited in this way. Otitis media alone is also negative. If a labyrinthine fistula complicate a suppurative otitis media, marked nystagmus may occur.

Minimal vestibular eye-movements with vertigo may occur with this test in rare cases of non-suppurative labyrinthine disease, in labyrinthine lues or trauma and in labyrinthine disease of unknown cause.

### vii. Vestibular Disturbances of Equilibrium

The way a patient tends to fall or to rotate in a vestibular disorder corresponds to the direction of the slow movement of his vestibular nystagmus, and the movement will occur in the same plane as that of the nystagmus. Thus if there be a horizontal nystagmus to the right (with slow movements toward the left), the reaction-movement will be in the horizontal plane toward the left—he will rotate to the left. In vertical downward nystagmus, the reaction-movement will be in the sagittal plane and backwards—he will fall backward. If there be rotary nystagmus to the right, he will fall to the left.

Change in the position of the head alters the direction of falling. Thus, if there be rotary nystagmus toward the right and the head of the patient be rotated 90° to the left, he will fall forward; rotate the head 90° to the right and he will fall backwards. As Bárány says, it is as though the direction of the fall "had grown fast to the head."

The vestibular reaction-movements vary greatly in different persons. Whereas one, with moderate nystagmus, will fall over like a stick, another, with extreme nystagmus, will stand as steady as a rock.

As tests of equilibrium, we ask the patient (1) to stand with his feet close together; (2) to shut the eyes; (3) to stand leaning forward or backward, and (4) to stand on one leg—an increasingly difficult series. A good routine is to begin by testing for a spontaneous Romberg (*q. v.*). If the patient sway, note whether a definite relation exists between the direction of the fall and any existing nystagmus. Next test the influence of rotation of the head on the direction of the fall. Finally, watch the effect of a caloric nystagmus upon the equilibratory disturbance.

Vestibular disturbances of equilibrium occur spontaneously during attacks of vestibular vertigo, and also along with the continuous nystagmus that sets in when the labyrinth is suddenly destroyed; in the latter case, if the nervous system be normal, the disequilibrium lets up in severity in a few days and soon passes off entirely.

The body muscles stand under the influence of the vestibular apparatus by way of Deiter's nucleus and the vestibulo-spinal paths descending from it to the anterior horns of the spinal cord. The influence of the position of the head upon the falling direction probably depends upon centripetal impulses from the muscles and joints of the head and neck, which pass to the vermis of the cerebellum and thence by a cerebellofugal path to Deiter's nucleus, either directly or by way of the nucleus of the roof.

Patients with pure cerebellar disease may fall much as do patients with vestibular irritation. But, in them, the direction of the fall is independent of nystagmus and of the position of the head (Bárány).

### viii. Vestibular Reaction-movements in the Extremities

A normal person with his eyes shut can stretch out one arm and hold it quietly very easily for about two minutes. Now if we produce a strong horizontal nystagmus toward the right by the caloric method of Bárány, and ask the patient to hold the arm outstretched and quiet, it will be observed that the arm deviates slowly and continuously to the left, the patient, as a rule, being unconscious of the deviation.

Still more striking, in some cases, than this arm-deviation is a modification of Gräfe's "touch test," the *"pointing error,"* elicited as follows (Bárány):

**Testing the Shoulder Joint by "Pointing Error" Test.**—The patient, with eyes closed, sits in front of the examiner, whose index-finger is held out horizontally in contact with the patient's forefinger, his arm outstretched. The patient then lowers the extended arm so that it rests on his knee, and is then told to raise it until it again comes in contact with the under-surface of the forefinger of the examiner. If the patient has a nystagmus to the right his arm will move out to the left and instead

of going directly up to the examiner's finger will pass it on the left ("pointing error").

Bárány emphasizes the necessity of avoiding letting the patient know how he responds to the test, so as to rule out the influence of suggestion. Thus if he fail to touch the examiner's finger, the examiner, himself, should place his own finger on that of the patient just after the error has been made, in order that the latter may not know of it.

The test can also be applied in the horizontal plane, to test for an "up" or "down" pointing error.

**Testing the Elbow Joint and Other Joints by the "Pointing Error" Test.**—The patient supports his elbow upon the arm of a chair, or, if in bed, upon a pillow, and performs the movements with his wrist held straight.

Similarly the hip and knee can be tested, sitting or lying, but the vestibular reaction-movements are less striking in the lower extremity than in the upper.

**Testing the Wrist Joint by the "Pointing Error" Test.**—The patient's forearm lies over the back of a chair and is held firmly there by the examiner. The patient then holds the index finger out straight, the other fingers clenched in the palm, and performs the movements, making as large excursions as possible up and down at the wrist joint.

If, in a normal person, a strong horizontal nystagmus to the right be produced, and no voluntary movements be made at the wrist, the arm hanging over the chair back with all the muscles completely relaxed, not the slightest movement will be observable. This proves that the appearance of the reaction-movements (in man) is indissolubly associated with voluntary innervations of the muscles concerned.

The pointing error to the left in horizontal nystagmus to the right occurs no matter whether the forearm is prone or supinated on the back of the chair. This is an important observation, since the voluntary innervation of the arm-muscles during the movements is entirely different in the two instances. It is obvious, therefore, that the innervations proceeding from the cerebral cortex determine to what muscles the vestibular impulses shall be sent (to the radial muscles in the one case, to the ulnar in the other). This determination, Bárány believes, takes place in the cortex of the cerebellum. Probably the collaterals given off from the pyramidal tracts in the pons go to the nuclei pontis, whence the impulses pass through the middle peduncle into the cerebellum to the opposite cerebellar hemisphere to reach the Purkinje cells. These Purkinje cells are also surrounded by terminals and collaterals from vestibular fibers. The path from the cortex of the cerebellar hemispheres to the spinal cord is by way of the brachium conjunctivum to the red nucleus of the opposite side and thence by the rubrospinal path of von Monakow to the cord. It seems not unlikely that the anterior-horn cells concerned in a given move-

ment are doubly innervated, first by fibers of the pyramidal tract, and, secondly, by the rubrospinal path carrying cerebro-cerebello-vestibular impulses!

Another interesting point is the observation that the pointing error to the left will occur not only with horizontal nystagmus to the right with the head upright, but with any form of nystagmus, provided the head be moved into a particular position. Thus if the head be bent down to the right shoulder and then be rotated to the left and so held, a vertical nystagmus upwards appears. A pointing error to the left will now occur. Though as regards the head the nystagmus is a vertical one, still, in space, it is a nystagmus to the right. Thus, if, during the existence of a nystagmus, the position of the head be changed, the direction of the pointing error will also be changed. As Bárány puts it, *the pointing error is a function of two variables; one is the vestibular stimulus, the other the head-position stimulus.* The two factors fuse in the cerebellar cortex.

An analysis of lesions of the cerebellar cortex indicates that the muscles are represented in the cerebellar cortex according to the joints they move and the movement-directions. *Each movement-direction for a joint is represented only once, but each joint and each muscle is represented at least four times in one cerebellar hemisphere. Each hemisphere is connected with the extremities of the same side.*

According to Bárány the center for moving the upper extremity medialward lies on the under surface of the cerebellum at its junction with the lateral surface.

For the details of localizing cerebellar and other lesions by means of the pointing error and other vestibular tests the original articles of Bárány should be consulted.

### ix. Anamnestic Vestibular Data

Rotary vertigo is the term used to designate the movement-sensations that accompany vestibular irritation. This rotary vertigo may assume either one of two forms: (a) sham-rotation of external objects, (b) sham-rotation of the patient's body. In both cases the sham-rotation, as a rule, is in the direction of the quick movement of the nystagmus, though not always.

Common concomitants are (1) darkening of the visual fields and color sensations, (2) nausea or vomiting, (3) sweating, (4) pallor, (5) palpitation, (6) difficulty in breathing, (7) fainting, (8) tremor.

Psychoneurotic patients seem especially prone to manifest these concomitant symptoms of vertigo, while patients with vertigo due to cerebellar disease or to disease of the pons or midbrain seem to be unusually tolerant of their vertigo. In local disease of the labyrinth, lessened sensibility to

vertigo is met with when the destruction is total; while in partial injury of the end-organ attacks of vertigo may continue for years in undiminished severity.

Bárány distinguishes two varieties of vertiginous attacks: (a) that with the brief nystagmus-attacks on quick movements of the head (*vide supra*) and (b) attacks lasting longer—sometimes for 24 hours—without apparent cause and usually accompanied by nausea or vomiting. In the latter, the direction and intensity of the nystagmus often change during the attack; the persistence of the vertigo is probably thus accounted for.

### x. The Rolling of the Eyes Opposite to the Lateral Flexion of the Head

This sign consists in a rolling movement of the eyes in a direction opposite to the movement of the head, on lateral flexion of the latter. This *Gegenrollung* of the eyes (Bárány) can be exactly measured by A. Schwarz's apparatus, but the use of the latter will doubtless be confined to specialists on the ear.

The method detects rolling movements invisible to the naked eye, but which may be associated with severe vertigo. Patients thought to be simulants may, with this apparatus, be found to have definite vestibular lesions.

### xi. Examination of the Vestibular Eye-reflexes in Cases with Eye-muscle Paralysis or Conjugate Deviation

It must be determined whether the eye-muscle paralysis is due to a lower motor neuron lesion or not; *i. e.*, whether the paralysis is due, on the one hand, to a lesion of the nucleus of origin or of the peripheral nerve, or, on the other, to a supranuclear lesion. In the former case vestibular stimulation will elicit no increase of movement in the paralyzed muscle, though in the other non-paralyzed eye-muscles vestibular nystagmus may be normally elicitable.

In conjugate deviation, due to lesion of the center, therefore, situated higher up than the eye-muscle nuclei, vestibular stimulation yields most interesting results of importance for diagnosis (Bielschowsky and Steinert, Bárány).

According to Bárány, one investigates the condition as follows: (a) Does spontaneous nystagmus exist? (b) On vestibular stimulation, does a nystagmus, associated equally with the two eyes, appear? (c) Is the quick movement of the vestibular nystagmus as quick as normal, or is it slowed? (d) In which direction can nystagmus be experimentally elicited, and in which not? (e) Does a deviation of the eyes appear in place of a nystagmus? (f) Can the eyes be voluntarily moved out of the position of conjugate deviation? (g) On doing this, does nystagmus appear? (h) During the vestibular stimulation, do both eyes show, or does only

one, an increase of motility in the direction of the slow movement of the nystagmus that would normally appear under the same stimulus, and how great is the increase? (i) During the vestibular stimulation, do

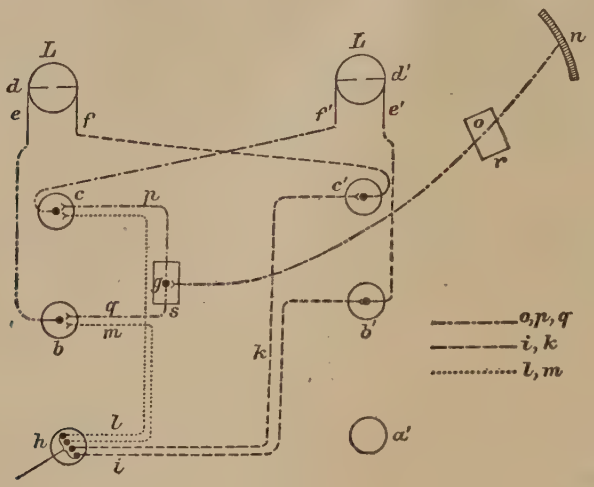


Fig. 528.—Diagram of Horizontal Nystagmus to the Left Released by the Left Semicircular Canals. a, a′ = Deiters' Nucleus, Left and Right; b, b′ = Nucleus VI, Left and Right; c, c′ = Nucleus III, Left and Right; d, d′ = Left and Right Eye; e, e′ = Rectus Ext., Left and Right; f, f′ = Rectus Int., Left and Right; g = Center for Looking to the Left; h = Left Vestib. Nerve; i = Vestibular Path (————), Crossing to Contralateral VI Nucleus; k = Vestibular Path (————), Crossing to Contralateral IV Nucleus; l = Vestibular Inhibitory Paths (.....) to Homolateral III Nucleus; m = Vestibular Inhibitory Paths (.....) to Homolateral VI Nucleus; n = Right Angular Gyrus (Cortex) Center for Voluntary Eye-movements to Left; o = Cortical Paths (—·—·—·) to Visual Center for Voluntary Eye-movements to Left; p = Supranuclear Paths (—·—·—·) from Left Visual Center to Homolateral III Nucleus; q = Supranuclear Paths (—·—·—·) from Left Visual Center to Homolateral VI Nucleus; r = Bilateral Lesions at r, Abolishing the Voluntary Eye-movements, Leaving Vestibular Nystagmus Intact (Pseudo-ophthalmoplegia of Wernicke); s = Bilateral Lesions at s, Abolishing Voluntary Eye-movements and the Quick Movements of Vestibular Nystagmus, Leaving the Slow Vestibular Movements Intact (Supranuclear Ophthalmoplegia of Bárány). (After R. Bárány, "Handb. d. Neur.," published by J. Springer, Berlin.)

both eyes show, or does only one, a diminution of motility in the direction of the quick movement of the nystagmus that would normally appear under the same stimulus, and how great is this?

### xii. Examination for Optic Nystagmus

Optic nystagmus can be elicited by rotation of a roll marked with black and white stripes in front of the eyes of the patient. Optic nystagmus appears on looking at the water from the deck of a moving ship or on looking out of the window of a railway train in motion.

Bárány suggests the interest of a study of optic nystagmus in the eye muscle paralyses of supranuclear and of cortical origin.

## (*b*) *Table of Vestibular Syndromes*

(Compiled by the author from R. Bárány's writings)

| Symptoms and Tests | I. Normal vestibular apparatus | II Circumscribed disease of r. vestib. app., or paresis of r. N. vestibuli | III R. labyrinth destroyed, or r. nervus vestibuli totally paralyzed; two days after injury | IV Same as in III, but eight days after injury | V Latent destruction of labyrinth, or total paralysis of r. nervus vestibuli (several months after) | VI Tumor of cerebello-pontile angle on r. side (destruction of labyrinth and cerebellar abscess on right) Type a | VII Same as VI; but Type b | VIII R. labyrinth normal; cerebellar abscess, or cerebellar tumor on right side |
|---|---|---|---|---|---|---|---|---|
| 1. Spontaneous nystagmus. | Absent; or slight rotary + horiz. N. to the r. on maximal deviation to the r. and slight rotary + horiz. N. to the l. on maximal deviation to the l. | Variable; may be absent. | Rot. + horiz. N. to the l.; very marked on looking in every direction. | N. to the l. less (N. to the r. often well marked). Decrease of N., more rapid with than without operation on the labyrinth. | Rot. N. to r. and rot. N. to l. slight, or absent. | Rot. + horiz. N. to r.; marked. | Rot. + horiz. N. to l. | Rot. + horiz. N. to r., to l., or to both sides of high grade; often abnormal forms (intra-cranial), e. g., vertical, diagonal rot. N. in one direction, and horizontal in the other. |
| 2. Spontan. N. behind the opaque spectacles on looking straight forward. | Absent. | Variable. | Horiz. N. to the l. | Horiz. N. to the l. (even when none present with spectacles off). | Negative. | Horiz. N. to r. | Horiz. N. to l. | Variable. |
| 3. Attacks of N. on quick movements of the head. | Absent; slight attacks occur in tobacco smokers. | On inclining head to r., usually rot. N. to r.<br>On inclining head to l. and forward, rot. N to l.<br>On inclining head forward, rarely vertical N. downward.<br>On inclining head back, rarely vertical N. upward. | Increase of spontan. N. | Negative. | Negative. | Increase of spontan. N. | As in VI. | Frequent. |
| 4. Caloric reactions:<br>(Head straight)<br>(*a*) Right ear, irrigated with cold water (25° C.).<br>(*b*) Right ear, irrigated with hot water (48° C.). | (*a*) Yields horiz. + rot. N. to the l.<br>(*b*) Yields rot. N. to the r. | (*a*, *b*) Normal response in both ears. | Right ear, negative (hot and cold).<br>Left ear, with cold = diminution of rot. N. to l., or rot. N. to r. | Right ear, negative.<br>Left ear, weak reaction. | Right ear, negative.<br>Left ear, very feeble; sometimes negative. | Right ear, negative.<br>Left ear, normal or lessened. | As in VI. | Right ear, marked N.<br>Bilat. simultaneous irrigation often shows over-excitability of diseased side (Ruttin). |
| 5. Rotation of body with opaque spectacles:<br>(*a*) 10 × r—head upright.<br>(*b*) 10 × l—head upright. | (*a*) N. to the l. 42″ average duration.<br>(*b*) N. to the r. 42″ average duration. | (*a*, *b*) Normal response. | ? | (*a*) 28″.<br>(*b*) 14″. | (*a*) 20″.<br>(*b*) 16″.<br>If N. to affected side longer than 25″, certainly no destruction. | ? | ? | Normal. |

(*b*) TABLE OF VESTIBULAR SYNDROMES—*Continued*

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 6. Galvanic nystagmus: 1-15 milliampère (*a*) Cathode in r. ear; anode in r. hand. (*b*) Anode in r. ear; cathode in r. hand. | (*a*) Rot. N. to r. (*b*) Rot. N. to l. | (*a*, *b*) Normal response. | ? | Not constant. | Positive or negative. | Usually no reaction on the side of disease. | As in VI. | Bilateral simult. stimulation with cathode causes N. to diseased side; with the anode, N. to opposite side. |
| 7. Fistula symptom. | Absent. | Negative. | Negative. | Negative. | Negative. | Negative. | As in VI. | Negative. |
| 8. Disturbances of equilibrium: (*a*) Spontaneous. (*b*) On expt'l rot. N. to r. | (*a*) Absent (neurasthenics may show dist. not vestib. in origin). (*b*) When head upright falls to l.; when head turned to r., falls forward; when head turned to l., falls backward. | Correspond to the nystagmus. | (*a*) Head upright, falls to l.; head turned to r., falls backward; head turned to l., falls forward. | Slight or absent. | Negative. | There are three possibilities: *a*, *b*, or *c*. (*a*) Vestibular (falling to left, head upright); (falling forward, head turned to r.); (falling backward, head turned to l.). (*b*) Cerebellar (fall independent of direction of N.; not influenced by change in position of head). (*c*) Expt'l N. from irrigating l. ear reveals disturbance of vestib. reactions since patient does not show typical dependence of direction of fall on direction of N., and, further, the direction of falling is not typically altered by change in head-position (cerebellar). | (*a*) As in VI, except that vestibular falling is to the left, with the head upright, etc. (*b*) As in VI. (*c*) As in VI. | As in VI. |
| 9. Hearing. | Normal; impaired; deaf. | Normal; or deaf. | Deaf on right (with noise-apparatus). | Same as for II. | Negative. | Deafness in the right. | As in VI. | Hearing present, but usually signs of lesion of internal ear. |
| 10. Vertigo. | Absent. | (*a*) On head movements, as in 3. (*b*) Long attacks without external cause, with N. to the r.; last up to 24 hrs. | Sham movement of ext. objects to l. Sham movement of own body to l. | Slight, or none. | Negative. | Present at beginning; absent later. | As in VI. | As in VI. |
| 11. Nausea and vomiting. | Absent on expt'l N.; often present in psychoneurotic states. | Often present with the vertigo. | Present. | Negative. | Negative. | Marked at first, later absent; indeed, there develops a sub-susceptibility to vestibular stimulation; even strong N. elicited from l. ear causes no vertigo and no nausea. | As in VI. | As in VI. |

(b) TABLE OF VESTIBULAR SYNDROMES—*Continued*

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 12. Position in bed. | Not noteworthy. | Lies usually on l. side, since turning to r. side causes vertigo. | Lies on healthy side. | Normal. | Normal. | Lies on the diseased side. | Lies on the healthy side. | Corresponds to the nystagmus. |
| 13. Ringing in the ears. | May, or may not, be present. | Present, or absent. | Present, or absent. | Same as for III. | Same as for IV. | Present, or absent. | As in VI. | As in VI. |
| Notes: | | | | | | If this syndrome is found along with chronic suppuration of the middle ear, one can at once diagnose total destruction of the labyrinth plus cerebellar abscess, since spontaneous N. to the diseased side in labyrinth-destruction (shown by absence of caloric N.) must have an intra-cranial cause.<br>Meningitis and cerebellar tumor can be ruled out by the other symptoms. If the syndrome be met with when the ear-drum is intact, tumor of the cerebello-pontile angle (N. acusticus) is probably present. | The diagnosis of an acute diffuse destruction of the labyrinth is first made.<br>If, after a few days observation, the N. has not diminished markedly in intensity (especially after operation on the labyrinth), or if it become more marked, an intra-cranial cause is certain. Further differential diagnosis as in VI. | In the differential diagnosis, circumscribed disease of labyrinth to be considered.<br>If the spontan. N., observed longer than 24 hrs., be undiminished, an intra-cranial cause is certain. The same is true of the abnormal forms of N., never observed in peripheral disease. In the remaining cases, the other symptoms will differentiate. |

### (c) *Vestibular Signs in Paralysis of the Supranuclear Apparatus for Conjugate Movements of Eyes (After R. Bárány)*

| Right sided, pure *Blicklähmung* | Bilateral, pure *Blicklähmung* |
|---|---|
| 1. Voluntary movements: Both eyes cannot be moved to the right beyond the middle line; to the left, the movements are free; the response is prompt and the movements quick. | 1. Voluntary movements: Those to the r. and to the l. are entirely abolished. |
| 2. Vestibular movements: On application of a stimulus that should cause horiz. N. to the r., there occurs, instead of this, a deviation of both eyes to the left, from which the eyes cannot voluntarily be set free. N. to the left can be elicited normally; while it lasts, the eyes can be moved, voluntarily, to the extreme right! | 2. Vestibular movements: Horiz. N. to the r. or to the l. cannot be elicited by any kind of vestibular stimulus. Instead of the N. to the r., both eyes undergo deviation to the l., the two eyes passing slowly to the extreme left, whence they cannot voluntarily be set free. Just the opposite occurs, when the stimuli that, normally, cause N. to the l. are applied. |

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## C. Examination of General Motility and of the Efferent Paths that Influence Striped Muscle

We must next learn how to examine the functions of the efferent, effector, or centrifugally conducting neuron systems that have an influence upon various structures in the body, and, through some of them, upon the external world. The nervous system is capable of altering the activities of the muscles (striped and unstriped), the secreting glands and possibly other structures. Of the millions of neurons making up the whole nervous system (cerebrospinal and sympathetic), only a few conduct impulses directly away from the nervous system to terminate in muscles and glands. These few, known as peripheral motor neurons, peripheral secretory neurons, etc., serve the purpose of transferring impulses from an enormous number of afferent and associative paths to the muscles and glands; they are *common terminal paths* (Sherrington) for a whole series of neural activities, and a study of these available terminal efferent channels is important for the understanding of the functions of the great number of reflex arcs that make up the nervous system as a whole (spinal reflexes, bulbar reflexes, cerebral reflexes, etc.).

These peripheral efferent or centrifugally conducting neuron systems can be directly influenced by the collaterals and terminals of peripheral afferent (or centripetally conducting) neurons, or by successively superimposed groups of such neuron systems, on the one hand, and by central efferent neuron systems and central associative neuron systems, on the other. These various central neuron systems, impinging upon the peripheral efferent neuron systems, are being gradually worked out anatomically and physiologically; we are now familiar with the structure and functions of many of them, though much more study must be undertaken for their further elucidation.

Clinically, we can already value:

1. The peripheral efferent neuron systems:
   (a) Those going to striped muscle;
   (b) Those going to the muscle of the circulatory apparatus (cardiac and vasomotor);
   (c) Those going to the smooth muscle of the respiratory, digestive and genito-urinary systems; and
   (d) Those going to the secreting glands.

The existence of

   (e) Peripheral neuron systems exerting a definite trophic influence upon various tissues of the body is assumed also, but definite proof for the existence of such neuron systems has yet to be brought.

2. A great central neuron system, the axons of which are known as the pyramidal tract, which throws the lower motor neurons going to striped muscle under the influence of the activities of the cerebral cortex; this great neuron system is composed of the so-called "upper motor neurons."

3. A complex group of other central neuron systems concerned in long reflexes, automatic and instinctive reactions, tonus maintenance, complicated and coördinated motor activities, vasomotor reactions, etc. Among these are included (1) those the axons of which make up the rubrospinal path (v. Monakow), extending from the nucleus ruber to the anterior horns, and (2) those the axons of which make up the vestibulospinal path, extending from Deiter's nucleus to the anterior horns.

The student, on beginning his acquaintance clinically with the functions of the efferent neuron systems, should confine himself to the better understood of these, and, later on, extend his study to the less well-known systems. In this elementary treatise, therefore, only the processes that are better understood will be dealt with.

In studying the afferent neuron systems, it has been noted that a large number of their functions go on below the threshold of consciousness, only a few of them being accompanied by definite conscious phenomena. The same is true of the functions of the efferent or centrifugally conducting neuron systems; a large part of them, including many of the reflex motor activities, the tonus maintenance in the general motor and in the vasomotor systems, the contractions of smooth muscle in the viscera, and the secretory activities, are largely infraconscious; some of them, like the respiratory movements and the movements of walking, are more or less

subconscious, and others, the so-called voluntary acts, we are definitely conscious of performing. We are able to judge of the functions of these efferent neuron systems in others only by observing the changes (or the effects of these) that occur spontaneously in the muscles and glands, or by experimentally bringing about such changes. Thus, on the observational side, we note the posture of the limbs and trunk, the facial expression, the evidences of glandular secretion, whereas on the experimental side we test the resistance to passive movements, the electrical condition of muscles and motor nerves, the reflex activities, and the motor and secretory reactions to stimuli applied to the afferent or centripetally conducting systems.

We shall take up, first, the examination of general motility and of the efferent paths that influence striped muscle.

The striped muscles of the body (with the exception of the muscles of the heart) are innervated by the "lower motor neurons," the cell bodies of which are situated in the anterior horns of the spinal cord and in the motor nuclei of the cerebral nerves. The axons of the lower motor neurons pass out through the ventral roots of the spinal nerves and through the motor roots of the cerebral nerves, to enter the peripheral nerve trunks (sometimes undergoing rearrangement in the plexuses), to end ultimately on the muscle fibers. The nervous impulses that cause contractions of these muscles—the reflex (lower and higher), the expressive (mimic, pantomimic or gesticulatory), the reactive and voluntary (defensive and aggressive)—are mediated by these lower motor neurons and by the central centrifugally conducting neurons that impinge upon them.

In accumulating data from which we draw inferences regarding the state of the motor path, we pay attention especially to the following:

1. The state of nutrition of the muscles as evidenced by their volume and by the electrical reactions (see electrodiagnosis) that they yield. Are any of the muscles atrophic? Does the electrical examination reveal a reaction of degeneration anywhere, or other anomaly?

2. The state of tonus of the muscles observable when testing passive motion. Is there evidence of atony, of hypotony, or of hypertony (rigidity, contracture)? Are there any peculiarities of body-form, or attitude, due to abnormal contractions of the muscles?

3. The behavior of the reflexes—deep and superficial. Are they exaggerated, diminished or perverted?

4. The evidences of abnormal motor irritation. Are any involuntary movements visible?

5. The behavior of the muscles during active (or voluntary) contractions initiated by the cerebral cortex. Is there inability to perform any of these movements (paralysis), or is the power lessened (paresis)? Does fatigue set in quickly (myasthenia)? Are the movements direct, precise and smooth, or do they show signs of being improperly coördinated

(ataxia)? Can complex motor acts be performed, or is there evidence of aphasia, agraphia or apraxia?

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## 1. The State of Nutrition of the Striped Muscles: Atrophy; Hypertrophy

The size of the voluntary muscles varies much among persons whom we call normal. Some have a well-developed musculature; in others the muscles are poorly developed. This variation within the domain of what we call normal depends in part upon inheritance, and in part upon the habits of the person. Muscles that are much used increase in size (*hypertrophy*); muscles that are but little used tend to decrease in size (*atrophy of inactivity*). Marked atrophy from inactivity is often seen in wasting diseases or in convalescence from acute disease.

In making the examination for the state of nutrition of the muscles, the whole naked body should be inspected. The physician must, from the examination of a large number of normal persons, be familiar with the normal form of the body and its musculature in order quickly to recognize deviations therefrom. Especial attention should be paid to inequalities in form on the two sides of the body, and, when inspection reveals an apparent deviation from the normal, the muscles should be carefully palpated and attention paid to the consistence (tense, relaxed, toughened). The presence or absence of fibrillary twitching (*q. v.*) in atrophied muscles should be especially looked for. When muscles appear to be enlarged, one should test their strength, since the increase in volume may be due to fat (pseudohypertrophy), and not to muscle tissue.

Small size of the muscles in general may be due to faulty development, to malnutrition, or, often, to lack of systematic exercise of the muscles. It is surprising how few people realize the importance of spending a few minutes every day in systematically contracting and relaxing the various muscle-groups of the body. A person that spends twenty minutes daily with J. P. Müller's "My System" or with S. Bennett's "Exercises in Bed" can keep his muscles active and firm, even in the absence of other forms of exercise.

Localized decrease in size (*atrophy*) is often most important for localizing diagnosis. When deviations from the normal are found, exact measurements should be made with a metal tape, the extremities on the two sides being held in the same position during the measurement. A few measurements will suffice. In the forearm and leg, one measures the maximal circumference, in the upper arm the circumference at its middle, in the thigh the circumference 12 cm. above the patella. It is to be kept in mind that normal differences of from ½ to 1 cm. may exist; moreover, differences of from ½ to 1 cm. are within the limit of error as measurements are ordinarily taken. Excision of small masses of muscle for histological examination are of little value clinically in the diagnosis of atrophy or hypertrophy. Most important for judgment as to the state of nutrition of the muscle is the test of its electrical excitability (*q. v.*). The state of the mechanical excitability of the muscle, though sometimes helpful, is of less importance (*q. v.*).

In nervous diseases, two main forms of muscular atrophy are met with: (a) *simple atrophy,* which develops slowly and is never extreme, and (b) *degenerative atrophy,* which develops more rapidly, is sharply localized, and leads to entire disappearance of the muscle-substance. In simple atrophy, innervation of the muscles is possible, at least through the lower motor neurons, but does not occur in normal amount. Here belong the different forms of "inactivity atrophy," due to bone and joint diseases, to long sojourn in bed, or to lesions of the upper motor neurons.

In degenerative atrophy, nerve impulses are entirely cut off from the muscles affected, and they exhibit on electrical examination the reaction of degeneration (*q. v.*)

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## 2. The So-called Tonus of the Striped Muscles: Atony; Hypertony; Contractures

Muscle-tonus is in part a variety of reflex, in part a conscious or subconscious innervation for the purpose of maintaining attitude. We understand by it the even, continuous, feeble state of contraction in which the voluntary muscles are during life constantly maintained, a state necessary in order that voluntary movements may be quickly and purposefully initiated. This tonus appears to be maintained largely by afferent stimuli coming from the muscles, tendons, fasciae and periosteum to the spinal

cord (protoceptive paths of Sherrington), where the impulses are transferred to the lower motor neurons, stimulation of which contracts the muscles concerned. Some of the tonus may arise from chemically stimulated central neuron systems, and some of it is consciously or subconsciously purposeful (attitude maintenance). Not all the muscles are equally contracted in tonus; thus, in the legs, the extensor muscles are more contracted than the flexors, and in general it would appear that the muscles in highest tonicity are those that have to maintain the normal attitude of the body against the influence of gravity. The intensity of the tonic innervation is dependent not only upon the innervations in the lower reflex arcs described, but also upon favoring and inhibiting influences arriving from higher neuron systems within the spinal cord and brain. Thus the tonus is increased greatly in certain muscles when the pyramidal tract is injured. Since the state of the muscle-tonus is a factor in the performance of active movements, it should be examined before the active movements are systematically tested. For tonus of cerebral origin, consult C. K. Mill's paper.

The muscle-tonus may be greater or less than normal. We form judgments concerning its degree by testing: (1) passive movements of the extremities, and (2) the reflexes, especially the deep reflexes.

Fig. 529.—Muscular Hypotony in Tabes.

### (*a*) *Tests of Tonus by Making Passive Movements*

We tell the patient to relax his limbs, to give them over entirely to the examiner, avoiding all tension, and we show him how an extremity, passively lifted, if relaxed, should fall by gravity. Some patients have difficulty in thus relaxing, in which case one must try to divert the attention by occupying the mind (multiplying, dividing, etc.). When we have assured ourselves of the absence of voluntary contraction, we seize an extremity, and move it in all directions and to the maximal extent that mechanical conditions of the joints, etc., permit. One makes the movement at first slowly, and afterwards more rapidly. The more firmly the limb is grasped on each side of a joint the easier it is, as a rule, for the patient to relax. If difficulty be experienced in performing these passive movements, we try to ascertain whether it is due to the muscular condition alone, or to joint changes (ankylosis, exostoses), or to other mechanical causes. The principal joints of the body should be successively tested in this way.

Normally the tonus-resistance of the limbs to passive movements is very slight, though palpable, and it can easily be overcome by a little

force. One learns by experience what the normal tonus is. Increase of tonus is known as *hypertony,* as abnormal *muscular rigidity,* or as a *spastic state.* The diminution of tonus is known as *hypotony;* its complete loss as *atony.*

Fig. 530.—Contracture in Left Spastic Hemiparesis. (Med. Service, J. H. H.)

Atonic or hypotonic muscles are met with in tabes (due to lesion of the sensory limb of the reflex arc), and in the flaccid paralysis (due to lesion of the motor limb of the reflex arc). They are softer and more relaxed in feel than normal. This permits of an abnormal lengthening of the muscles and of abnormally great excursions of the limbs on passive and active movements of the joints. If the muscles of the legs be atonic, they can sometimes (as in some cases of tabes) be placed about the patient's neck. In hypotony, the joints, instead of the limitation of excursion due to tonus met with in health, may exhibit a passive mobility like that demonstrable in a cadaver.

In markedly hypertonic states (such as those met with, for example, in spastic paraplegia and in other forms of pyramidal-tract lesions), the rigidity may be so great as to make passive movements almost impossible. When the hypertony is slight, it may become noticeable only on rapid performance of the passive movements, inasmuch as brusque passive movements reflexly increase the tonus and unmask a latent hypertony; thus, such a sudden flexion of the leg at the knee will sometimes reveal a hypertonic state that would otherwise go unrecognized.

A peculiar hypertony of unknown origin is to be seen in the *rigidity of Parkinson's disease;* the rigidity is often a more marked feature than the tremor of the disease; it is responsible for the clumsiness of movement of the patient and for the masklike rigidity of the face.

What is known as *waxy flexibility* (flexibilitas cerea), a condition

often met with in catatonic or cataleptic states, must be regarded as a peculiar alteration of muscle-tonus; it is, in all probability, a condition brought about by cerebral influence. On performing passive movements, the extremities that are in a state of waxy flexibility retain any attitude given to them, even when left to themselves for a considerable time. They behave as though they were made of plastic wax (*catatonic* or *cataleptic rigidity*); there seems to be a loss of voluntary power over motility, psychogenic in its origin. In children, and in hypnosis, this condition is sometimes simulated when the patient believes that he cannot or dare not interfere with the passive movements made (so-called *pseudoflexibilitas*).

Another extraordinary manifestation of muscle-tonus is that met with in those rare cases known as Thomsen's disease (*myotonia congenita*), in which the patient, on attempting to perform a movement, is often unable to do so because of a suddenly appearing hypertony in the muscles concerned when he attempts to initiate a movement; or, having closed his fist, he cannot quickly reopen it. An opposite condition of extreme flaccidity and atony of the muscles, especially of the lower extremities (*amyotonia congenita*) is sometimes met with in small children. Here the hypotony, like that in progressive muscular atrophy, seems to be due to a primary "motor" anomaly, not to injury of the sensory limb of the arc as in tabes. In certain joint diseases, and in some forms of idiocy (mongolism), a hypotony due to relaxation of the joint-ligaments is met with.

Recently, a peculiar condition has been described in which a marked hypertony with spasm affects certain groups of muscles, especially those of the pelvic girdle, causing the so-called "dromedary gait"; the condition is known as *tortipelvis* or *dystonia musculorum deformans*. A physician of my acquaintance suffers from it. It is apparently closely related to spastic torticollis.

When active and passive motility of a limb or joint has been permanently interfered with through hypertony or muscle shortening, we say that a *contracture* exists. When the hindrance to movement can be removed by influences that diminish the tonus or contracted state of the muscles (*e. g.,* manipulation in narcosis, or in the warm bath), the condition is called an *active contracture;* but when the hindrance is due to actual muscle-shortening rather than contraction, it is called a *passive contracture.* An active contracture lasting a long time may give rise, finally, to a passive contracture from organic shortening.

Recently, a strong reaction against prevalent conceptions of muscle-tonus has set in. It is maintained (1) that there is no such thing as a general "contraction of the muscles when at rest," (2) that what has been called tonus is a coördinative performance that calls forth a certain attitude by means of finely graded contractions. This new doctrine, which would avoid the term "tonus" altogether, has a bearing upon the explanations of ataxia (M. Lewandowsky).

### (*b*) *Anomalies of Form and Attitude* (*Local and General*)

As a result of general and local disturbances of tonus (or of the special coördinative functions hitherto described as tonus) seen in cases of muscular paralysis, muscular atrophy and contracture, certain characteristic alterations of the form and attitude of various parts of the body arise. Some of these will here be mentioned.

In the domain of the extremities we meet with (1) the *bird-arm* or *bird-leg,* due to reduction in size of the distal portions of the extremities from atrophy of the muscles of the fore-arm or leg; (2) the *claw-hand,* from atrophy of the interossei with contracture of the long flexors and extensors of the fingers (ulnar paralysis); (3) the *simian hand* or *ape-hand,* due to atrophy of the thenar eminence (progressive muscular atrophy, median paralysis); (4) the *preacher-hand,* due to contraction of the extensors of the fore-arm and the long flexors of the fingers, with paralysis of the small muscles of the hand (pachymeningitis cervicalis); and (5) *wrist-drop,* due to radial paralysis (lead-poisoning). Here belong also (6) *flat-foot,* (7) *equino-varus,* and (8) the various forms of *club-foot,* dependent upon neuromuscular lesions.

In the domain of the head and trunk may be mentioned (1) the *tapir-lips,* due to weakness of the M. orbicularis oris (myopathies); (2) the "starched face" or *"mask"* in Parkinson's disease; (3) the *eye-conditions* in Basedow's disease; (4) the *rotation of the scapula* in paralysis of the trapezius; (5) the *winglike projection of the scapula* in serratus paralysis; (6) the *scoliosis, lordosis* and *kyphosis* of the spine met with in various conditions; and (7) the *hernia-like projection* on both sides of the hypogastric region above Poupart's ligament, brought out on straining, in paralysis of the lower abdominal muscles (poliomyelitis, lower thoracic hematomyelia).

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## 3. The Deep Reflexes or So-called Tendon Reflexes

A second important method of ascertaining the state of "muscle-tonus" consists in the demonstration of an increase or diminution of the activity of the reflexes, especially of the deep reflexes, though it must be remembered that hypertony and exaggeration of the reflexes do not always go parallel with one another.

The tendon reflexes depend also upon reflex arcs, of which the afferent limbs correspond to the protoceptive systems (afferent impulses from (a) muscle, and (b) bone, excited by the tap on the tendon) and the efferent limbs to lower motor neurons of corresponding segments. The muscular contractions in these reflexes are characterized (1) by their very short duration, the movement being due usually to a single contraction, and (2) by a latent period, which is so brief that some have even doubted, erroneously, the reflex character of the movement. Like the tonus of the striped muscles, the deep reflexes are under the influence of neuron systems within the spinal cord and brain that favor or inhibit them.

Clinically, the most important deep reflexes are: (a) the knee-jerk; (b) the ankle-jerk; (c) the tarsophalangeal reflex (Bechterew, Mendel); (d) the periosteal-radial reflex; (e) the biceps reflex; (f) the triceps reflex; and (g) the jaw-jerk.

Table of Deep Reflexes

| Reflex. | Method of Eliciting. | Result. | Segmental Level. |
|---|---|---|---|
| Knee-jerk | Tapping patellar tendon. | Contraction of M. vastus medialis; extension of leg. | $L_3$ and $L_4$ |
| Ankle-jerk | Tapping tendo Achillis. | Contraction of calf-flexors; extension of foot | $S_1$ and $S_2$. |
| Tarso-phalangeal. | Tapping lateral tarsus or metatarsus | Flexion of toes II-V | $L_5$—$S_2$. |
| Periosteal-radial | Tapping radius just proximal to styloid process. | Contraction of M. brachio-radialis; flexion of fore-arm held midway between pronation and supination. | $C_5$ and $C_6$. |
| Biceps | Tapping biceps tendon. | Contraction of M. biceps; flexion of fore-arm | $C_5$ and $C_6$. |
| Triceps | Tapping triceps tendon. | Contraction of M. triceps; extension of fore-arm | $C_7$ to $Th_1$. |
| Jaw-jerk | Tapping examiner's thumb over chin, patient's mouth half open | Contraction of masseter muscles; jaw closes | N. trigeminus (pars motorius). |

### (*a*) *The Knee-jerk or Patellar Reflex*

This reflex, which consists of a contraction of the M. quadriceps on tapping the patellar tendon, may be tested either in the recumbent or in the sitting position, the former, if convenient, being preferable.

**In the Recumbent Position.**—We flex the patient's knee to an obtuse angle and support it from beneath with our left hand, the patient's heel resting on the bed. With our right hand we seek the patellar tendon, and, having found it, give it a brief tap with a heavy hammer (preferably Déjerine's), and observe whether or not a contraction in the M. quadriceps, and especially in the M. vastus medialis, a little above the knee, follows. If the reflex be active, the whole M. quadriceps may contract and cause extension of the leg. When less active, the contraction of the muscle beneath the skin can be observed, though care must be taken not to confuse this with the simple jar of the skin and muscle propagated from the blow given to the tendon. Should no contraction result, we must make sure that the leg has not been held tense by the patient. When the leg is properly relaxed it should fall at once by gravity when the supporting hand in the popliteal space is suddenly withdrawn. Some patients have much more difficulty than others in relaxing their limbs, though usually, after a little instruction, they learn how to do it. A great deal depends upon the experience, skill and tact of the examiner. Where the difficulty is marked one may resort to *reinforcement* (Jendrassik), the patient clasping his hands, and, on command, pulling powerfully without letting go while the examiner taps the patellar tendon.

**In the Sitting Position.**—The patient may sit (1) in a chair, with one knee crossed over the other; (2) in a chair, with the soles of the feet flat on the floor, the legs almost perpendicular, or (3) on a table, with the legs hanging over the edge. While the patellar tendon is tapped the examiner may place his left hand upon the thigh above the knee, in order to feel the contraction, or, better, he may tap his own left forefinger placed over the patellar tendon and feel the response as an increased tension of the tendon. In *Laufenauer's method of reinforcement* the patient sits with the soles of his feet flat on the floor, while the examiner, with the left hand, grasps the patient's quadriceps. The patient is then told to grasp the left upper arm of the examiner with one hand and to squeeze suddenly on command, the examiner at the same time performing the tap. By this method one can tell whether or not the patient is really directing his attention to the act of reinforcement. In *Schönborn's method of reinforcement* the patient squeezes the left hand of the examiner, while the latter taps the tendon with the hammer held in his right hand. A jerk that is feeble often becomes much stronger with reinforcement.

Experience teaches one what to expect as a normal response when testing for the knee-jerk, and, also, what is exaggeration, what diminution.

Before one decides that the knee-jerk is absent, repeated tests should be made, and the absence of mechanical hindrances (diseased knee-joint, dislocated patellar tendon, ununited fracture of the patella, burial of the tendon in fat, excessive edema) ensured.

When the knee-jerk is much exaggerated, a slight tap may cause a marked kick, and a spread of the contraction to other muscles. Furthermore, instead of a brief single contraction, a group of contractions rapidly succeeding one another may result, causing a clonus of the M. quadriceps. In such cases a *patellar clonus* can often be elicited by seizing the patella with the thumb and forefinger from above, pressing it suddenly downwards, and holding it in its depressed condition (yielding, perhaps, a little); the M. quadriceps is set into clonic contractions that continue until the patella is relaxed. Along with a patellar-clonus, or in place of it, and having the same significance as regards a pyramidal-tract lesion, is the *crossed adductor reflex*. When this is present, the tap on the patellar tendon is followed by a contraction of the adductor muscles of the opposite thigh, best seen when this thigh is slightly abducted and rotated lateralward (Hinsdale and Taylor, P. Marie).

The absence of the knee-kick, sometimes known as *Westphal's sign,* is of great diagnostic importance as a sign of organic disease of the nervous system, as will be seen later. In a normal person the knee-jerk can always be elicited. It is occasionally absent as a stigma of degeneration. It may be temporarily absent in persons otherwise healthy when they are fatigued or exhausted; thus Knapp and Thomas often found it diminished and occasionally absent in long-distance runners after the race. The knee-jerk may disappear for a short time after an epileptic seizure or during chloroform narcosis; occasionally it is absent during acute infections, especially during pneumonia in children.

The knee-jerk often disappears early in tabes (lesion of sensory limb of arc); it also disappears in multiple neuritis and in poliomyelitis (lesion of motor limb of arc), provided the disease attacks the region of the nervous system in which the reflex-arc lies. The knee-jerk often disappears temporarily after a cerebral insult (apoplexy), owing to shock or diaschisis. As a rule the knee-jerk is permanently absent after total transverse lesion of the spinal cord above the level of the arc (*Bastian's law*); the reason for this is not known.

### (*b*) *The Ankle-jerk*

(*Heel Phenomenon, Achilles Tendon Reflex*)

The patient kneels in a chair, the feet relaxed and hanging free over the margin of the seat. The tendo Achillis is then gently tapped with a percussion hammer. Normally, plantar flexion of the foot results, owing

to contraction of the calf-muscles. Tested in this way, the ankle-jerk is practically always present in healthy persons, including children.

The ankle-jerk may be absent in the same conditions as those in which the knee-jerk is lost. This reflex is fully as important as the knee-jerk; indeed, it usually disappears in tabes before the knee-kick goes.

Fig. 531.—Testing the Achilles Reflex.

If the ankle-jerk be increased there may result from the tap not only a single contraction, but clonic contractions known as *ankle-clonus* (foot-phenomenon or foot-clonus). When this is present it may be most beautifully demonstrated if the patient be seated in a chair, his leg flexed slightly at the knee, the latter supported by one hand of the examiner, while with the flat of the other hand the ball of the foot is pressed suddenly upward into a position of dorsal flexion; the foot should not be held too rigidly in the dorsally-flexed position by the examiner or the clonus will not occur. One tries stronger and gentler dorsal flexion until a maximal clonus is obtained. In *true ankle-clonus* (*épilepsie spinale parfaite* of Babinski) the contractions of the calf-muscles occur rhythmically four to six times per second, and continue as long as the foot is held dorsally flexed; in the *false ankle-clonus* (*épilepsie spinale fruste* of Babinski), met with in hystericals, and occasionally in health, the oscillations are more frequent, they are not present at every examination, and they do not occur

in complete relaxation of the muscles. In some instances it is extremely difficult to differentiate the false from the true clonus.

### (*c*) *The Tarsophalangeal Reflex* (*Bechterew-Mendel*)

On tapping the lateral part of the dorsum of the foot, especially over the cuboid bone or the base of the third metartarsal, there occurs in health and in functional nervous disorders a dorsal flexion of all the toes except the great toe; in lesions of the pyramidal tract there occurs a plantar flexion of the toes, often accompanied by spreading of the toes. It is a far less reliable reflex than the Babinski phenomenon (*q. v.*). A special toe-reflex—plantar flexion and abduction after a brief volar tap—has been described by Rossolimo in pyramidal tract lesions after the third week.

### (*d*) *The Periosteal Radial Reflex*

The patient's elbow is flexed at a right angle, held midway between pronation and supination, so that the thumb is upward. The surface of

Fig. 532.—Testing the Periosteal Radial Reflex. (Flexion of the Fore-arm on the Arm.)

the radius, just above its styloid process, is tapped with the percussion hammer, and the examiner watches for a contraction of the M. brachio-radialis (supinator longus) near the elbow.

### (*e*) *The Biceps Jerk*

The patient's loosely flexed elbow is supported in the palm of the examiner's left hand, the thumb of this hand pressing upon the biceps tendon at the bend of the elbow. The examiner then taps his own thumb with the percussion hammer. The response of the patient's tendon is felt under the thumb, and there is an increased flexion of the fore-arm.

### (*f*) *The Triceps Jerk*

The examiner supports the patient's upper arm in a horizontal position, the fore-arm hanging loosely, the elbow flexed at a right angle. The

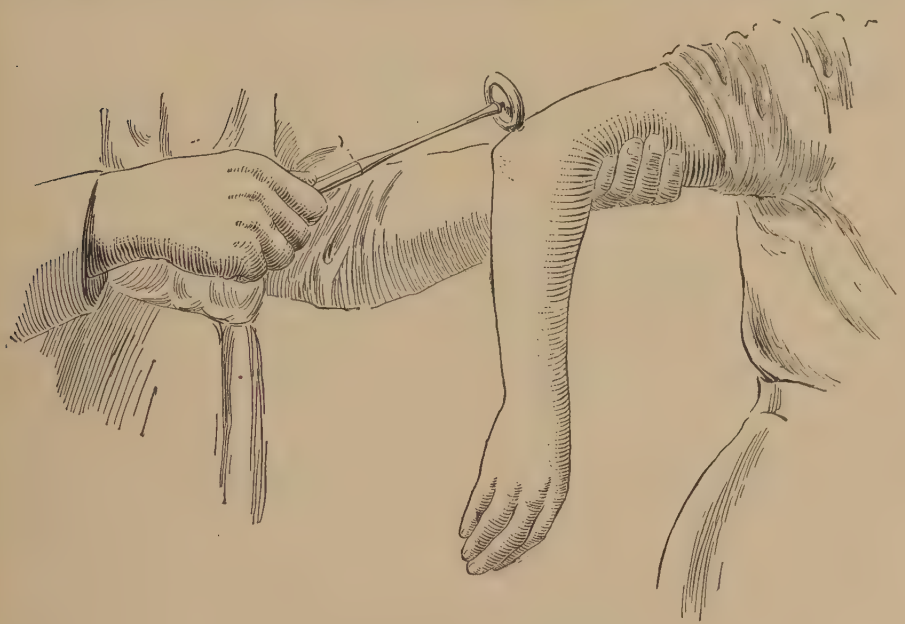

Fig. 533.—Testing the Triceps Reflex.

triceps tendon is then struck with a percussion hammer; the response consists in a visible contraction of the M. triceps, with more or less extension of the forearm.

The deep reflexes in the upper extremities are somewhat less constant than in the lower, even in health, and, unless markedly exaggerated, or constantly absent, are of but little help in clinical diagnosis.

A *hand-clonus,* which can sometimes be produced by suddenly lifting the fin-

gers hanging loosely in the flexed position, is, like ankle-clonus, an indication of exaggeration of tonus. A forearm-clonus and a pectoral clonus have also been described (Bouchard).

### (*g*) *The Jaw-jerk* (*Masseter Reflex*)

The patient's chin, his mouth half open and his masticatory muscles relaxed, is supported by the index finger of the examiner's left hand, the thumb resting upon the front of the chin, beneath the lower lip. The thumb is then tapped with a percussion hammer. Normally this gives rise to a slight contraction of the masseter muscles, with elevation of the jaw. Another method of testing the jaw-jerk is to tap with a percussion hammer, the finger, the handle of a spoon or a table-knife placed upon the lower teeth.

In marked hypertony, mere depression of the lower jaw with the fingers may give rise to a clonus, the so-called *jaw-clonus,* or masseteric clonus.

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## 4. The Superficial Reflexes

*(Skin and Mucous Membranes)*

By superficial reflexes are meant the motor responses elicited by stimulating certain areas in the skin and mucous membranes (*reflexogenous zones*). They are normally more easily elicited in earlier than in later life. A large number of such reflexes have been described, but only those most often used in clinical work will be mentioned here.

TABLE OF SUPERFICIAL REFLEXES

| Reflex. | Method of Eliciting. | Normal Result. | Segmental Level. |
|---|---|---|---|
| Plantar. | Partially flex hip and knee, rotating extremity slightly lateralward; gently stroke sole of foot from behind forward. | Contraction of all toe-flexors, extensors of foot, flexors of knee and hip. | $L_5$—$S_2$. |
| Abdominal: | | | |
| 1. Uppermost epigastric (diaphragm). | Stroke skin of chest downward between 3rd and 7th rib, or irritate the nipple. | Retraction in the middle line near the xiphoid process and as far as the first tendinous inscription of rectus. | $T_7$—$T_9$. |
| 2. Supraumbilical. | Stroking skin of abdomen from 7th rib down as far as level of umbilicus. | Tension of abdominal wall on side of stimulus from costal margin down as far as umbilical level, including upper parts of M. rectus. | |
| 3. Infraumbilical. (Hypogastric) | Stroke skin from level of umbilicus to Poupart's ligament. | Tension of abdominal wall on side of stimulus from level of umbilicus to Poupart's ligament. | |
| Cremasteric. | Stroke upper part of thigh on its medial aspect. | Retraction of testicle. | $L_1$—$L_2$. |
| Superficial anal. | Pricking skin of perineum. | Contraction of M. sphincter ani externus. | $S_5$ and coccygeal. |
| Bulbocavernosus. | Pinch dorsum of glans penis. | Palpable contraction of M. bulbocavernosus. | $S_3$—$S_4$. |
| Gluteal. | Stroking skin of buttock. | Contraction of M. gluteus maximus. | $L_4$—$L_5$. |
| Scapular. | Stroking skin in interscapular region. | Contraction of scapular muscles. | $C_5$ to $T_1$. |
| Palatal or uvular. | Touch uvula, or soft palate, with glass rod. | Elevation of uvula and soft palate. | |
| Swallowing. | Touch root of tongue with rod. | Contraction of muscles of deglutition. | |
| Gagging. | Tickle posterior wall of pharynx. | Contraction of pharyngeal muscles; occasionally vomiting. | |
| Coughing. | With aid of laryngoscope, touch laryngeal mucous membrane with probe. | Cough. | N. vagus. |
| Sneezing. | Tickle mucous membrane of nostril with feather. | Sneezing. | Motor part of N. trigeminus. |
| Corneal and conjunctival. | Touch cornea or conjunctiva gently with glass rod or head of pin. | Quick and powerful closure of lid from contraction of M. orbicularis. | Sensory part of N. trigeminus; N. facialis. |
| Optic-lid. | Threaten eye with fist. | Closure of lid. | N. opticus; N. facialis. |

The reflexes in the table given above need no especial description. By far the most important, clinically, are the plantar reflex, the cremaster reflex and the abdominal reflexes.

### (a) *The Plantar Reflex*

The abnormal responses in the domain of this reflex are of the greatest help in differential diagnosis. In lesion of the pyramidal tracts (upper motor neurons), with integrity of the lower motor neurons and sensory paths, instead of the normal flexor response of the great toe to plantar stimulation, a remarkable pathological extensor response, known as *Babinski's phenomenon of the toes,* is obtained. On stroking, with a dull needle

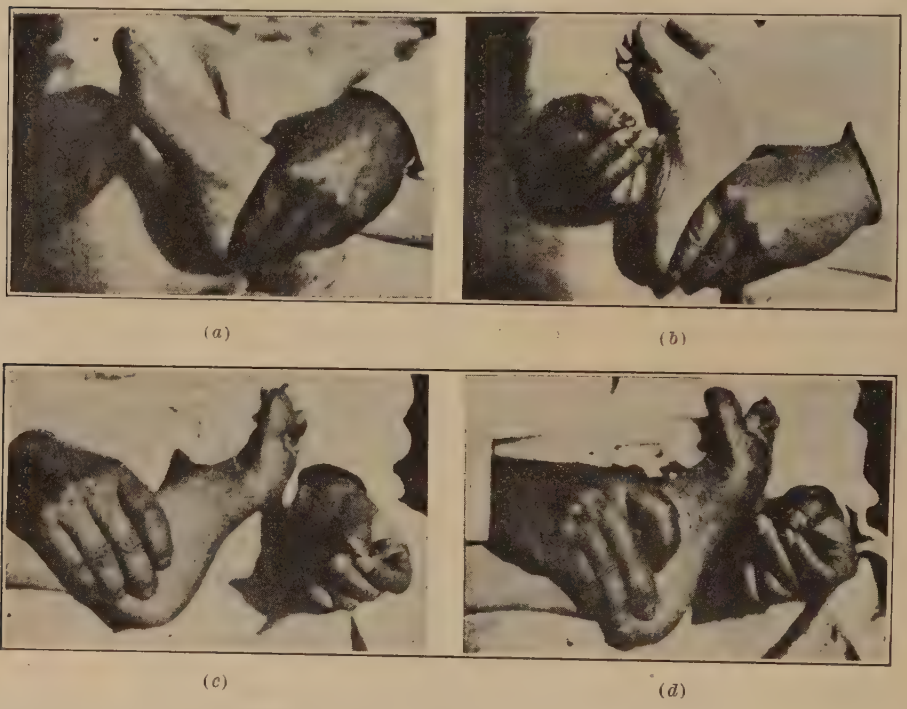


Fig. 534.—(*a*) Left-sided Organic Hemiplegia of a Year's Duration Photograph of the Right (Normal) Foot at Rest; (*b*) Foot Represented in Figure Photographed at the Moment of Stimulating the Sole with a Needle. This Illustrates a *Normal* Response; (*c*) Subject Whose Right Foot Was Shown in Figure (*a*). Photograph of the Left Foot at Rest; (*d*) Foot Represented in Figure (*c*). Photographed at the Moment of Stimulating the Sole with a Needle. "Toe Phenomenon." This is Ordinarily Known as a "Positive Babinski" and Indicates a Lesion of the Pyramidal Tract. (After J. Babinski, "Gazette des Hôpitaux," published by Bureaux d'abonnement, Paris.)

or with a latch-key, the sole of the foot, especially from behind forward along its lateral margin,[1] or transversely over the distal part of the sole, there results a slow but strong dorsal flexion of the great toe (M. extensor hallucis longus), accompanied either by plantar or dorsal flexion of the

[1] Stroking the medial margin sometimes results in plantar flexion when stroking the lateral margin yields dorsal flexion.

other toes if they move at all, and often followed by spreading of the toes apart, especially by marked abduction of the little toe (so-called *fan-sign*). Dorsal flexion of the foot occasionally accompanies, and flexion of the knee and hip, with marked contraction of the tensor fasciae femoris, often accompany, the phenomenon of the toes (*flight-reflex, shortening reflex*). If a "tickle response" be so marked as to interfere with the test, one may try lowering the sensibility to tickling by rubbing ice over the plantar surface of the foot. It is to the slow hyperextension of the great toe that the examiner's attention should always be directed. In some instances

1. Foot in Repose.

2. Foot at Moment of Excitation.

Fig. 535.—Abduction of the Toes ("Fan Sign") of the Right Foot in Spastsic Paraplegia. (After J. Babinski, "Revue Neurologique," published by Masson et Cie, Paris.)

one cannot decide definitely whether the response is positive or negative; the response is "equivocal." One should test the reflex then on several different occasions.

Babinski's sign has been found positive in the most different lesions of the pyramidal tract, including (1) recent and old hemiplegias, due to cerebral hemorrhage, embolism or thrombosis; (2) tumor cerebri; (3) meningo-encephalitis; (4) Jacksonian epilepsy; (5) epidemic cerebrospinal meningitis; (6) multiple sclerosis; (7) amyotrophic lateral sclerosis; (8) Friedreich's ataxia; and (9) some cases of combined sclerosis in pernicious anemia. It is never positive in hysteria without associated organic lesion (Buzzard).

When the Babinski phenomenon is positive one can usually demonstrate also the presence of the *leg phenomenon of Oppenheim;* one runs the pulp of the thumb, or the handle of a percussion hammer, rather vigorously along the medial surface of the leg over the tibia, or just behind its posteromedial edge, passing from above downward to the medial malleolus. When the sign is positive there is an active dorsal flexion of the great toe

and of the foot, due to contraction of the M. tibialis anticus and the M. extensor hallucis longus (sometimes of M. extensor digitorum communis and of the Mm. peronei). In normal persons, the same summation of stimuli results only in plantar flexion of the toes or of the foot, or in no reflex movement at all.

In young infants (up to the seventh month) the normal response to plantar stimulation is of the extensor type, probably owing to incomplete development of the pyramidal tract; but after early childhood—certainly after the second or third year—the constant presence of an extensor response to plantar stimulation indicates an organic lesion involving the pyramidal tract. There is, in my experience, no test more reliable than Babinski's for differentiating organic from functional disorders.

Similar in significance to the Babinski phenomenon and to Oppenheim's sign is *Gordon's paradoxical flexor reflex.* The patient lies on his back, or sits resting his foot upon a chair, with muscles completely relaxed; the examiner, standing beside him, presses deeply with the tips of his fingers in the middle of the calf. In lesions of the pyramidal tract, extension of the great toe, or of all the toes, results. The plantar reflex may, like other superficial reflexes, be entirely absent in functional or organic anesthesia of the skin, of the sole of the foot, or, in lesions, of the lower motor neurons innervating the muscles concerned.

### (*b*) *The Cremaster Reflex*

The method of eliciting this is indicated in the preceding table of superficial reflexes.

The cremaster reflex is almost constantly present in healthy persons (97-99 per cent).

An exaggeration of this reflex is, as yet, of no clinical importance, but its absence, especially on one side, is a very important sign of pyramidal tract injury. In the coma immediately following the apoplexy causing a hemiplegia, the reflex may be abolished on the hemiplegic side (Redlich), sometimes on both sides; the cremasteric reflex is, however, occasionally retained, despite the existence of a hemiplegia.

### (*c*) *The Abdominal Reflexes*

These, like the other cutaneous reflexes, are best elicited by a summation of stimuli (*e. g.,* drawing the handle of a hammer or a needle in a line across the skin, either parallel to or at right angles to the middle line). The response is a brief contraction of the abdominal muscles on the side stimulated, often with a corresponding displacement of the umbilicus toward the same side.

The response occurs always under normal conditions, provided the person examined does not hold the abdominal muscles tense. It is often

temporarily absent during intra-abdominal disease, especially in appendicitis and in typhoid fever (H. D. Rolleston).

Absence of the abdominal reflexes in young people, especially when associated with weakness of the abdominal muscles, points strongly to multiple sclerosis (v. Strümpell, E. Müller), an observation I have many times had opportunity to confirm.

The relations of the abdominal reflexes to the cerebral cortex are interesting. They are especially influenced by cortical lesions. A person cannot elicit his own abdominal reflexes (psychic cortical influence). Again, in hysterical or suggested anesthesia of the skin of the abdominal wall, the reflex may not be elicitable.

It seems certain that the reflex depends on superimposed arcs, a lower arc made up of cord and peripheral nerves, and one or more higher arcs made up of long paths, including the cerebral cortex within the arc. Hence abolition of the abdominal reflex may be met with, not only in lesions of the pyramidal tract, but also in peripheral lesions (neuritis, pressure on nerve-roots, etc.). In tabes the reflex may be either abolished, or in cases with hyperesthesia of the skin of the trunk, exaggerated.

A number of reflexes (including the sphincter reflexes and the pupillary reflexes), the motor limbs of the arcs of which belong to the autonomic nervous system, will be referred to further on.

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## 5. Testing the Active Movements

### (*a*) *Preliminary Orienting Examination*

Here again it is well to make, first, a quick, general and somewhat superficial examination for purposes of orientation, testing, (1) several simple voluntary movements by command, (2) certain of the more complicated coördinated movements, such as (a) touching the nose with the finger or (b) the knee with the heel, (3) the maintenance of equilibrium with the eyes shut, (4) the speech (including writing), (5) the gait of the patient and (6) certain praxic phenomena. If this first examination for orientation reveal abnormalities, then a systematic and complete investigation of the whole motor sphere should be undertaken according to the tables given at the end of this section.

In testing the active movements, we first exclude (a) pain-preventing movements and (b) the existence of mechanical hindrances to movement (joint-stiffness, scars, contractures).

#### i. Simple Movements

When the patient responds to our request to perform various movements, we note any limitation in the extent of the movement and the slowness or quickness with which it is performed. We test also the strength of the movement by requiring the patient to perform it against resistance made by ourselves. We compare especially the power on one side with that on the other, remembering, of course, that the power of the right arm is usually stronger than the left in the proportion of about 5:4. We keep in mind that, in voluntary movements, groups of muscles (synergists) are commonly used together, the agonists or protagonists contracting vigorously, the antagonists simultaneously relaxing or contracting, only in sufficient degree to grade the movement. In these complicated synergistic movements individual muscles may not act as a whole; certain parts of

individual muscles only contract. In an exact analysis, therefore, of motility, it is desirable to test, in as far as this is possible, the functions of the individual muscles, as well as the capacity for purposeful synergistic movements.

Special attention should be paid to any abnormal tendency to fatigue on the repetition of voluntary movements. A patient may be able to perform a movement once or twice relatively well, but on further repetition the movements grow weaker until, finally, they can no longer be performed at all. In myasthenia gravis this abnormal fatigability of muscles often appears first in the eye-muscles or in the muscles of mastication (chewing beef-steak).

Fig. 536.—Paralysis of M. serratus magnus and M. rhomboideus. (Med. Service, J. H. H.)

One asks the patient to wrinkle up his forehead, to frown, to close the eyes tightly (against resistance of examiner's thumb and forefinger), to open the eyes wide, to laugh, to show the teeth, to grip the jaws tightly together, to make chewing movements, to put out the tongue and to move it from side to side. The eye-movements are quickly and roughly tested by asking the patient to follow the examiner's finger moved in various directions. Convergence is tested by bringing the finger close to the nose as the patient focuses upon it. If any abnormality in eye-movement is found, one tests each eye separately in order to distinguish disturbances of associated movements from monocular anomalies.

In the extremities the patient's power of flexion, extension, abduction and adduction, medial and lateral rotation are tested for each joint, in as far as each joint is capable of undergoing such movements. The examiner takes firm hold of the limb with his hands, one hand proximal to the joint to be tested, the other distal from it, and asks the patient to make

movements against resistance. The strength of the hand may be tested by the grip or by the dynamometer; the latter is scarcely necessary, as one soon learns to estimate a normal grip.

In the region of the trunk especial attention should be paid to the size of the trapezius on each side, and one should note whether or not the scapulae stand at the same level and if the deltoid be normally prominent. The patient should be able to lift each arm to a vertical position. On testing the forearm for supination and pronation the shoulder should be fixed, in order to make sure that the movements are made at the elbow and not in the shoulder-joint. The movements of the spine are tested by asking the patient to bend forward, backward and to each side, and to rotate his trunk in each direction. On examining the lower extremity, besides testing the movements of the various joints in all directions, one inspects closely (1) the anterolateral surface of the leg to see whether or not the M. tibialis anticus and the M. digitorum communis project normally, and (2) the back of the leg, to see if the calf-muscles are of normal volume. In the hands, the thenar and hypothenar eminences should always be inspected, as well as the interosseous spaces on the backs of the hands.

### ii. Coördinated Movements of the Extremities

For rough orientation two tests suffice: (1) the finger-nose test, and (2) the heel-knee test.

**The Finger-nose Test.**—The patient is asked to close his eyes, and, with his arm extended to one side, slowly to make a movement by which he touches the end of his nose with the point of his index finger. One requires him to make the movement at different speeds, and notices (1) whether the finger reach its goal or not, (2) whether it attain it by the shortest course, and (3) whether any marked tremor or oscillation be exhibited, especially as the goal is approached (intention-tremor).

One may modify this test by asking the patient to touch the index finger of one hand with the same finger of the other, or to place the tip of his index finger in the bell of a stethoscope held at some distance from him. One compares the ability of the patient to make the movement with his eyes open with that shown when the eyes are shut.

We may also ask the patient (1) to bring a glass brim full of water to his mouth, (2) to button and unbutton his coat or his collar, and (3) to thread a needle.

**The Heel-knee Test.**—The patient, lying on his back, is asked to close his eyes and to touch the knee of one leg with the heel of the other, and then to pass the heel slowly down the front of the shin to the ankle.

The patient may also be asked to hold, with his eyes closed, each foot steady at a certain distance above the bed (static test), or he may be

required to make a circle with his foot, or to designate certain geometrical figures therewith (dynamic test).

The *pointing error test* has been described under Tests of Vestibular Function.

### iii. Coördination of Muscles of Trunk (Romberg's Symptom)

Any marked disturbance of equilibrium will probably be shown by swaying on standing or sitting. Slighter disturbances will be detected by removing from the patient some of the normal aids to equilibrium. One asks him to close his eyes and to stand with the medial margins of his feet close together. A healthy man can stand steadily, presenting only a very slight and slow oscillation. Marked swaying or inability to stand is known as *Romberg's symptom.* One also asks the patient to rise from a sitting position, and to sit down from a standing position, with his eyes closed. The maintenance of equilibrium can be made more difficult still by requiring the patient to hold his arms straight out in front of him, to incline his head to one side, or to hold his head strongly flexed, extended, or rotated.

Ataxia on walking, if slight, may appear if the patient be required to make, suddenly, a right about turn.

### iv. Speech and Writing

The anamnesis will usually reveal whether or not any speech disturbance is present. We note (1) how the patient expresses himself, and (2) whether or not he understands what we say to him. We ask him to write his name and address, and note any abnormalities. If a speech disturbance is obvious, or be suspected, the special examination for the organs of speech is made (see Aphasia, further on).

### v. Gait

We ask the patient to walk, first slowly, then quickly, and we observe closely the gait. Does he walk straight forward? Are the two legs moved alike? Does he walk with a broad or narrow base? Is the gait stamping or flopping? Does he swing one leg out from the side or drag his toe? Can he turn quickly and walk in the opposite direction? (see section dealing with pathological gaits).

### vi. Certain Rough Praxic Tests

The examiner asks the patient to perform certain acts. For rough orientation the following will suffice: (1) beckoning; (2) lighting a candle; (3) conducting an orchestra; (4) grinding a coffee-mill, followed by turning a hand-organ; (5) sealing a letter; (6) sharpening a lead pencil; (7) opening a pocket-knife (see Apraxia).

### (*b*) *Systematic Analysis of Active Movements*

A thorough examination of all the muscles of the body accessible to the clinician is necessary if one wishes to avoid overlooking important motor disturbances. There are so many muscles and movements that the examiner should not attempt to keep them all in his head, but should follow a definite scheme, such as that presented in the following table:

## Scheme for Exact Investigation of Active Movements[1]

### A. Head, Neck and Trunk

### *I. Movements of Face and Jaw*

| | Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|---|
| 1 | Wrinkling the forehead transversely; elevation of eyebrows | M. epicranius | N. VII | |
| 2 | Frowning | M. corrugator | N. VII | |
| 3 | Shutting the eyes tight | M. orbicularis palp. | N. VII | |
| 4 | Enlarging the nostrils; wrinkling up nose | M. nasalis; M. depressor septi | N. VII | |
| 5 | Drawing angle of mouth to side; laughing; showing teeth | M. quadratus lab. sup.; M. zygomaticus, etc. | N. VII | |
| 6 | Drawing angles of mouth downward | M. quadrat. lab. inf.; M. triangularis | N. VII | |
| 7 | Elevating lower lip | M. mentalis | N. VII | |
| 8 | Pointing the lips; whistling | M. orbicularis oris | N. VII | |
| 9 | Moving the external ear | Mm. auriculae | N. VII | |
| 10 | Chewing; biting | M. masseter; M. temporalis | N. $V_3$ | |
| 11 | Movement of mandible lateralward and forward | M. pterygoid. med. et. lat. | N. $V_3$ | |

### *II. Movements of the Eyes*

| | Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|---|
| 1 | Elevation of upper lid | M. levator palp. sup. | N. III | |
| 2 | Looking upward and medialward | M. rectus superior | N. III | |
| 3 | Looking upward and lateralward | M. obliquus inferior | N. III | |
| 4 | Looking medialward | M. rectus medialis | N. III | |
| 5 | Looking lateralward | M. rectus lateralis | N. VI | |
| 6 | Looking downward and medialward | M. rectus inferior | N. III | |
| 7 | Looking downward and lateralward | M. obliquus superior | N. IV | |
| 8 | Associated movement of two eyes to left and to right | | | |
| 9 | Convergence of eyes | | | |
| 10 | Accommodation for near vision | M. ciliaris | Autonomic | |

### *III. Movements of Tongue, Soft Palate, Pharynx and Larynx*

| | Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|---|
| 1 | Protrusion and retraction of the tongue; movement of the tongue to each side | Intrinsic mm. of tongue; M. genioglossus; M. hyoglossus; M. styloglossus | N. XII | |
| 2 | Movements of soft palate on intonation | M. tensor palati; M. levator veli palati; M. palatoglossus; M. palatopharyngeus | N. IX; X | |
| 3 | Swallowing | The pharyngeal muscles in addition to the palatine | N. IX; X | |
| 4 | Elevation of epiglottis | M. thyreo-aryepiglotticus | N. laryng. sup. | |
| 5 | Movements of vocal cords | Laryngeal muscles | N. recurrens | |

[1] Compiled by the author from Oppenheim, Jamin, Flatau *et al.*

## *IV. Movements of Head, Neck and Trunk*

| | Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|---|
| 1 | Bending head and neck forward (Flexion) | M. rectus capitis anterior; | Nn. cerv. i-iii | $C_1$ |
| | | M. longus capitis; | Nn. cerv. i-iv | $C_1$—$C_4$ |
| | | M. sternocleidomastoideus | N. XI | $C_2$—$C_3$ |
| 2 | Bending head and neck backward (Extension) | M. splenius capitis et cervicis; | Nn. cerv. i-iv | $C_2$—$C_8$ |
| | | M. semispinalis capitis et cervicis | Nn. cerv. i-iv | $C_1$—$C_2$ |
| | | M. rectus capitis post. maj. et min. | Nn. cerv. i-iv | $C_1$—$C_2$ |
| 3 | Rotating head to one side | M. sternocleidomastoideus | N. XI | $C_2$—$C_3$ |
| | | M. obliquus capitis inferior | Nn. cerv. i-iii | $C_2$ |
| | | M. longus colli | Nn. cerv. i-iii | $C_2$—$C_8$ |
| 4 | Flexing head lateralward to shoulder | M. rectus capitis lateralis | Nn. cerv. i-iv | $C_1$ |
| 5 | General attitude of spine | M. spinalis cervicis | Nn. cerv. i-iv | |
| 6 | Extension of spine; bending trunk backward | M. iliocostalis dorsi et lumborum | Nn. thoracales | $T_2$—$L_1$ |
| | | M. longissimus dorsi | Nn. thoracales | $T_2$—$T_{12}$ |
| 7 | Flexion of spine; bending trunk forward | M. rectus abdominis, etc. | Nn. thor. viii-xii | $T_5$—$T_{12}$ |
| 8 | Rotation of the spine to right or to left | M. semispinatus dorsi | Nn. thoracales | $T_4$—$T_9$ |
| 9 | Latero-flexion of spine; bending trunk to side | M. quadratus lumborum | Plexus lumbalis | $T_{11}$—$L_2$ |
| 10 | Contraction of diaphragm (abdominal breathing; Litten's sign; visible on fluoroscopy) | Diaphragm | N. phrenicus | $C_3$—$C_5$ |
| 11 | Thoracic breathing | Mm. scaleni; | Nn. cervicales | $C_4$—$T_{12}$ |
| | | Mm. intercostales | Nn. thoracales | |
| 12 | Abdominal compression (bearing down; coughing; loud crying) | Diaphragm with closed glottis; | | $C_3$—$C_5$ |
| | | Abdominal muscles; | | $T_5$—$L_1$ |
| | | Muscles of pelvis floor | | $S_3$—$S_4$ |

## B. Shoulder Girdle and Upper Extremity

## *I. Shoulder Blade*

| | Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|---|
| 1 | Raising the scapula, drawing it upwards | M. trapezius | N. XI, Nn. cerv. iii, iv | $C_2$—$C_4$ |
| | | M. levator scapulae | N. dorsalis scapulae | $C_3$—$C_5$ |
| 2 | Drawing scapula toward middle line | Mm. rhomboidei | N. dorsalis scapulae | $C_4$—$C_5$ |
| 3 | Fixation, and rotation, of scapula | M. serratus anterior | N. thorac. longus | $C_5$—$C_7$ |

## *II. Shoulder-joint*

(Movements of Upper Arm)

| | Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|---|
| 1 | Lifting arm forward or at the side to a horizontal level; abduction of arm | M. deltoideus | N. axillaris | $C_5$—$C_6$ |
| 2 | Adduction of arm, and drawing it down | M. pect. maj. et min. (when arm is outstretched) | N. thorac. ant. | $C_5$—$C_8$ |
| | | M. latissimus dorsi (downward and backward) | N. subscapul. | $C_6$—$C_8$ |
| 3 | Rotation lateralward | M. supraspinatus | N. suprascap. | $C_5$ |
| | | M. infraspinatus | N. suprascap. | $C_5$—$C_6$ |
| | | M. teres minor | N. axillaris | $C_5$ |
| 4 | Rotation medialward | M. subscapularis | N. subscap. | $C_5$—$C_6$ |
| | | M. teres major | N. subscap. | $C_6$ |

## *III. Elbow-joint*

(Movements of the Fore-arm)

| | Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|---|
| 1 | Flexion: | | | |
| | (*a*) In supination | M. biceps brachii | N. musculocut. | $C_5$—$C_6$ |
| | | M. brachialis | N. musculocut. | $C_5$—$C_6$ |
| | (*b*) In half-pronation | M. brachioradialis | N. radialis | $C_5$—$C_6$ |
| 2 | Extension | M. triceps | N. radialis | $C_6$—$C_7$ |
| 3 | Pronation | M. pronator quadratus | N. medianus | $C_6$—$T_1$ |
| | | M. pronator teres | N. medianus | $C_6$—$C_7$ |
| 4 | Supination | M. biceps brachii | N. musculocut. | $C_5$—$C_6$ |
| | | M. supinator (brevis) | N. radialis | $C_5$—$C_7$ |

## *IV. Wrist-joint*

(Movements of the Hand)

| | Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|---|
| 1 | Volar flexion | M. flexor carpi radialis | N. medianus | $C_6$—$C_7$ |
| | | M. flexor carpi ulnaris | N. ulnaris | $C_8$ |
| 2 | Dorsal flexion (=Extension) | M. extensor carpi rad. long. | N. radialis | $C_6$—$C_7$ |
| | | M. extensor carpi rad. brev. | N. radialis | $C_6$—$C_7$ |
| | | M. extensor carpi ulnaris | N. radialis | $C_7$—$C_8$ |
| 3 | Bending hand radialward | M. extensor carpi rad. long. | N. radialis | $C_6$—$C_7$ |
| | | M. flexor carpi rad. | N. medianus | $C_6$—$C_7$ |
| 4 | Bending hand ulnarward | M. flexor carpi ulnaris | N. ulnaris | $C_8$ |
| | | M. extensor carpi ulnaris | N. radialis | $C_7$—$C_8$ |

## *V. Movements of Fingers II-IV*

| | Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|---|
| 1 | Flexion of the proximal phalanges | Mm. interossei | N. ulnaris | $C_7$—$C_8$ |
| | | Mm. lumbricales | Nn. uln. et. med. | $C_7$—$C_8$ |
| 2 | Flexion of the middle and terminal phalanges | M. flexor digitor. sublim. | Nn. med. et uln. | $C_7$—$T_1$ |
| | | M. flexor digitor. profund. | Nn. med. et uln. | $C_7$—$T_1$ |
| 3 | Extension of proximal phalanges | M. extensor digitor. com. | N. radialis | $C_6$—$C_8$ |
| | | M. extensor indicis | N. radialis | $C_6$—$C_8$ |
| 4 | Extension of middle and terminal phalanges | Mm. interossei | N. ulnaris | $C_7$—$C_8$ |
| 5 | Spreading the fingers (abduction) | Mm. interossei dorsales | N. ulnaris | |
| 6 | Adduction of the fingers | Mm. interossei volares | N. ulnaris | |

## *VI. Movements of the Thumb*

| | Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|---|
| 1 | Flexion of the metacarpus and of the prox. phalanx | M. flexor poll. brevis | Nn. med. et uln. | $C_6$—$C_7$ |
| | | M. abductor poll. brevis | N. medianus | $C_6$—$C_7$ |
| 2 | Flexion of terminal phalanx | M. flexor poll. longus | N. medianus | $C_6$—$C_7$ |
| 3 | Extension of metacarpus and of both phalanges | M. extensor poll. longus | N. radialis | $C_6$—$C_7$ |
| | | M. extensor poll. brevis | N. radialis | $C_6$—$C_7$ |
| 4 | Abduction of metacarpus | M. abductor poll. long. | N. radialis | $C_6$—$C_7$ |
| 5 | Opposition | M. opponens pollicis | N. medianus | $C_6$—$C_7$ |

### *VII. Movements of the Little Finger*

| Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|
| 1 Flexion | Mm. flexor digit. prof. et subl.<br>M. flexor digit. min. brev. | Nn. med. et uln.<br>N. ulnaris | $C_7$—$T_1$<br>$C_8$ |
| 2 Extension | M. extens. digit. min. prop. | N. radialis | $C_7$—$C_8$ |
| 3 Abduction | M. abductor digit. min. | N. ulnaris | $C_8$—$T_1$ |
| 4 Opposition | M. opponens digit. min. | N. ulnaris | $C_8$ |

## C. Pelvic Girdle and Lower Extremity

### *I. Hip-joint*

(Movements of the Thigh)

| Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|
| 1 Flexion | M. iliacus; M. psoas | Nn. lumbales | $L_1$—$L_4$ |
| | M. sartorius; M. rectus femoris | N. femoralis | $L_2$—$L_4$ |
| | M. tensor fasciae latae | N. femoralis | $L_4$—$L_5$ |
| 2 Extension | M. glutaeus maximus | N. glut. inf. | $L_5$—$S_1$ |
| 3 Abduction | Mm. glutaeus med. et min. | N. glut. sup. | $L_4$—$S_1$ |
| 4 Adduction | M. pectineus | N. obturat. | $L_2$—$L_3$ |
| | Mm. adduct. long., brev., et magn. | N. obturat. | $L_2$—$L_4$ |
| | M. gracilis | N. obturat. | $L_2$—$L_4$ |
| | M. obturator ext. | N. obturator. | $L_3$—$L_4$ |
| | M. pyriformis | N. glut. sup. | $S_1$—$S_2$ |
| 5 Lateral (external) rotation | M. quadratus femoris | N. ischiadicus | $L_4$—$S_1$ |
| | Mm. gemelli | N. ischiadicus | $L_4$—$S_1$ |
| | M. obturator int. | N. ischiadicus | $L_5$—$S_2$ |
| 6 Medial (internal) rotation | Mm. glutaeus med. et min. | N. glut. sup. | $L_4$—$S_1$ |
| 7 Sitting up, when lying on the back | Abdominal muscles; Iliopsoas | | |
| 8 Fixation of the pelvis on the thighs: | | | |
| In front | M. glutaeus maximus | N. glut. inf. | $L_5$—$S_1$ |
| At the side | Mm. glutaeus med. et min. | N. glut. sup. | $L_4$—$S_1$ |

### *II. Knee-joint*

(Movements of the Leg)

| Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|
| 1 Flexion | M. biceps femoris | N. ischiadicus | $L_5$—$S_2$ |
| | M. semitendinosus | N. ischiadicus | $L_4$—$S_1$ |
| | M. semimembranosus | N. ischiadicus | $L_4$—$S_1$ |
| | M. gracilis | N. obturator. | $L_2$—$L_4$ |
| | M. sartorius | N. femoralis | $L_2$—$L_3$ |
| 2 Extension | M. quadriceps femoris | N. femoralis | $L_4$—$S_1$ |

### *III. Ankle-joint*

(Movements of the Foot)

| Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|
| 1 Dorsal flexion: | | | |
| (*a*) Elevation of medial margin of foot | M. tibialis anticus | N. peroneus | $L_4$ |
| (*b*) Elevation of lateral margin of foot | Mm. peroneus long. et brev. | N. peroneus | $L_5$—$S_1$ |
| 2 Plantar flexion | M. gastrocnemius | N. tibialis | $L_5$—$S_2$ |
| | M. soleus | N. tibialis | $L_5$—$S_1$ |
| 3 Adduction with elevation of medial margin of foot (supination) | M. tibialis posticus | N. tibialis | $L_5$—$S_1$ |
| 4 Abduction; pronation | M. peroneus brevis<br>(Also other Mm. peron. and M. ext. dig. l.) | N. peroneus | $L_5$—$S_1$ |

### *IV. Movements of Toes II-IV*

| Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|
| 1 Flexion: | | | |
| (*a*) Of proximal phalanges.... | Mm. interossei et lumbricales | N. tibialis | $S_1$—$S_2$ |
| (*b*) Of terminal phalanges..... | Mm. flexor digit. long. et. brev. | N. tibialis | $L_5$—$S_2$ |
| 2 Extension..... | Mm. extensor digit. long. et brev. | N. peroneus | $L_4$—$S_1$ |
| 3 Spreading the toes (abduction)... | Mm. interossei dorsales | N. tibialis | $S_1$—$S_2$ |
| 4 Adduction..... | Mm. interossei volares | N. tibialis | $S_1$—$S_2$ |

### *V. Movements of the Great Toe*

| Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|
| 1 Flexion: | | | |
| (*a*) Of the proximal phalanx.. | M. flexor hallucis brevis | N. tibialis | $S_1$—$S_2$ |
| (*b*) Of the distal phalanx..... | M. flexor hallucis longus | N. tibialis | $L_5$—$S_2$ |
| 2 Extension: | | | |
| (*a*) Of the proximal phalanx.. | M. extensor hallucis brevis | N. peroneus | $L_4$—$L_5$ |
| (*b*) Of the distal phalanx..... | M. extensor hallucis longus | N. peroneus | $L_4$—$L_5$ |
| 3 Abduction..... | M. abductor hallucis | N. tibialis | $L_5$—$S_1$ |
| 4 Adduction..... | M. adductor hallucis | N. tibialis | $S_1$—$S_2$ |

### *VI. Movements of the Little Toe*

| Active Movements | Muscles | Nerves | Segments |
|---|---|---|---|
| 1 Flexion..... | M. flexor digit. min. brev..... | N. tibialis | |
| 2 Abduction..... | M. abductor digit. min. | N. tibialis | $S_1$—$S_2$ |
| 3 Opposition..... | M. opponens digit. min. | N. tibialis | $S_1$—$S_2$ |

### D. The Movements of the Eyes and Their Innervation

| Nerve | Muscles | Active Movement |
|---|---|---|
| *N. III; N. oculomotorius*.... | 1 M. levator palpebrae | 1 Lifts the upper lid. |
| | 2 M. rectus superior | 2 Moves the cornea and the visual line chiefly upward and slightly medialward; slight wheel-rotation of upper half of eye nasalward. |
| | 3 M. rectus inferior | 3 Moves the cornea and the visual line downward and slightly medialward; slight wheel-rotation of lower half of eye nasalward. |
| | 4 M. rectus medialis | 4 Moves the cornea and the visual line medialward; adduction, horizontal pull nasalward. |
| | 5 M. obliquus inferior | 5 Pulls the posterior, lateral inferior quadrant medialward and downward; moves the cornea and the visual line upward and lateralward, and causes wheel-rotation, so that the lower half of the cornea rolls medialward; the upper half lateralward. |
| *N. IV; N. trochlearis*..... | 6 M. obliquus superior | 6 Pulls the lateral, upper, posterior quadrant of the eyeball upward and medialward; moves the cornea and the visual line downward and lateralward, and causes wheel-rotation, so that the upper half of the eyeball rolls nasalward. |
| *N. VI; N. abducens*..... | 7 M. rectus lateralis | 7 Moves the cornea and the visual line lateralward; abduction, horizontal pull lateralward. |

### (c) *Rules for Detecting Paralysis of the Eye-muscles*

1. Examine the width of the lid-slits; if the upper eyelid hang too low and the patient cannot raise it (except by contracting the M. epicranius), there is *ptosis*, due to paralysis of the M. levator palpebrae.

2. Ask the patient to look at an object at a distance. Normally, the axes of the two eyes will be parallel; if they be not parallel, *squint* or

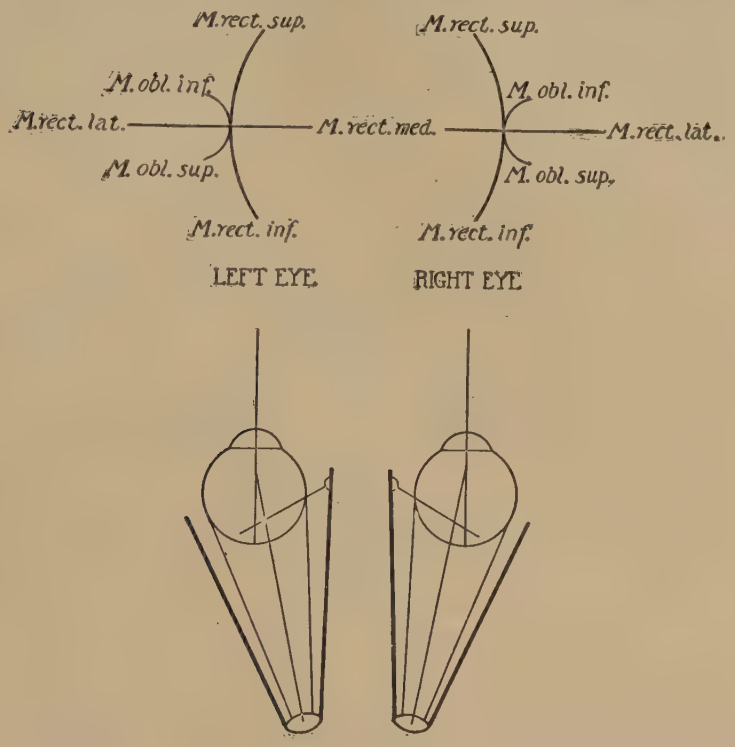


Fig. 537.—Effects of Contraction of the External Muscles of the Eye. (After Heine.)

*strabismus* exists. This may be due to a paralysis of an eye-muscle (*strabismus paralyticus*), or there may be no eye-muscle paralysis (*strabismus concomitans*).

3. Ask the patient to look spontaneously to the right, to the left, up and down, and note whether the eyeballs make the full excursions normally seen.

4. Ask the patient to follow the examiner's finger, moved in the several directions; occasionally, eye-movements can thus be performed that do not occur on spontaneous looking.

5. Ask the patient to look at a distance, and then at the examiner's finger held close to the face (convergence test).

In 3, 4 and 5 the angle of a paralytic strabismus becomes enlarged on movements involving the function of the paralyzed muscle; if a muscle be totally paralyzed, the eye does not move at all in the direction it should follow on normal contraction of the muscles; if it be only paretic, it moves less than normal with gradual increase of the angle of the squint. In strabismus concomitans, the angle of the squint does not change on movements of the eyes in any direction.

6. Ask the patient to fix on an object first with the paralyzed eye (the other covered with the hand), and then with the healthy eye (the paralyzed eye covered); it will be observed that the deviation is greater in the eye

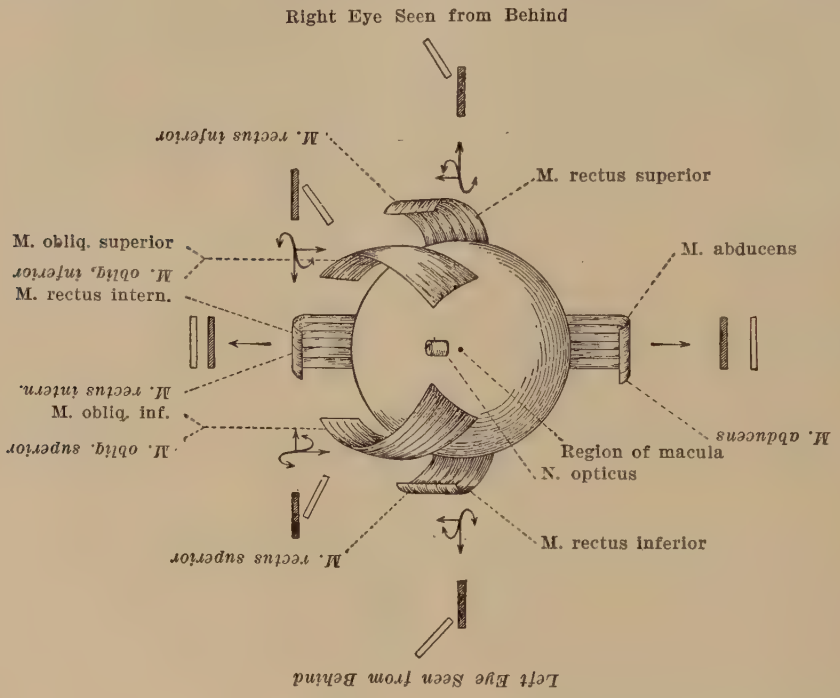


Fig. 538.—Diagram of Movements of the Eyeball and of Diplopias Due to Paralysis of the Eye-muscles.—In the Upright Position the Diagram is for the Right Eye; in the Diagram Held Upside Down, the Italics Are for the Left Eye. The Arrows Near the Muscles Indicate the Components of the Direction of Action of the Individual Muscles. The Arrows Pointing to the Rectangles Indicate the Double Images, the Black the Real Image, the White the False One; the Latter is Dislocated as Regards the Former in the Direction Indicated by the Arrow. After O. Veraguth, "Die klin. Untersuch. Nervenkranker," published by J. F. Bergmann, Wiesbaden.)

excluded from vision when the affected eye is fixed (secondary deviation) than *vice versa*.

7. Ask the patient, his head being in the position for looking straight forward, to fix on an object with the affected eye, the object being placed in a part of the visual field that, for fixation, requires contraction of the enfeebled muscle. Then ask him to touch the object with his finger. The

abnormally strong innervation required to make the weak muscle contract sufficiently to fix on the object, deceives the patient into thinking that the object is situated further from the middle line than it really is; he projects it falsely in space. Thus, for example, if his M. rectus lateralis of the right eye be paralyzed, he will think the object lies farther to the right than it does, and on attempting to touch it (*touch test*), will place his finger to the right of it.

8. Make a systematic test for the existence of double images (*diplopia*); this test is far more delicate than the other tests for strabismus, and may reveal eye-muscle weakness, not discoverable otherwise.

We take the patient in a dark room, cover one eye with a red glass, the other with a green glass, and ask him to look at a long, lighted candle which we hold at a distance of 9 or 10 feet from the patient and move into all nine parts of the visual field. We note (1) whether double images occur; (2) in what positions of the candle they occur; (3) how the two images—the false seen by the paralyzed eye, the true by the sound eye—stand in relation to one another; whether on the same side of the true image as the eye affected, or crossed; whether the false image is on a horizontal level with the true, or is higher, or lower; whether the false image has its upper end tilted toward, or away from, the true.

The kind of diplopia that will appear in the several paralyses, can be easily arrived at by analysis if one knows the action of the several muscles on the eyeball and considers what abnormal position the eyeball must assume.

As Axenfeld emphasizes, it is absurd to learn by heart the squints and the double images for all the different paralyses. The two following rules are, however, helpful:

(a) The deviated eye in a squint always dislocates its (false) image into the half of space opposite to that of the squint.

Thus in lateralward squint (strabismus divergens): false image medialward (nasalward, crossed); in medialward squint (strabismus convergens): false image lateralward (temporalward, uncrossed); in downward squint (strabismus deorsum vergens): false image upward; in upward squint: false image downward.

(b) The false image becomes displaced in the direction toward which the paretic or paralyzed muscle normally draws the eyeball.

Thus, in paralysis of the M. rectus medialis: medialward (nasalward, crossed, corresponding to the strabismus divergens); in paralysis of the M. rectus lateralis: lateralward (uncrossed, corresponding to the strabismus convergens); in paralysis of the M. rectus superior: upward, slightly medialward (crossed), and the tops rotated slightly nasalward, vertical and slightly crossed diplopia.

In all diplopias, the patient, in order to avoid the double images, tends to hold the head so that in looking straight forward the weak muscle is innervated as little as possible; thus for every eye-muscle paralysis there is a definite head-attitude.

For exact measurements of slight muscular insufficiencies (heterophoria), various instruments (phorometer, tropometer, clinoscope, phoroptometer) have been devised for the use of specialists on the eye.

### (*d*) *The Movements of the Tongue*

We study the following movements of the tongue, as worked out by Flesch: (1) protrusion of tongue (bilateral action of Mm. genioglossi); extreme protrusion requires also the action of the Mm. pterygoidei to shove the mandible forward; (2) turning the protruded tongue to one side (M. genioglossus of opposite side); (3) retraction of the tongue (Mm. styloglossus, hyoglossus, and chondroglossus); (4) turning the tongue in the mouth to one side (M. styloglossus of the same side); (5) feeling the lateral surface of the mouth cavity with the tongue (simultaneous contraction of the homolateral M. styloglossus and the heterolateral M. genioglossus); (6) depression of the tongue (Mm. genioglossi and hypoglossi); (7) elevation of the tongue (Mm. styloglossi and palatoglossi); (8) narrowing and broadening the tongue (Mm. transversalis et longitud. linguae).

## 6. Disturbances of Motility (Striped Muscles)

Total inability to perform active movements is known as *paralysis* or *akinesis*. When the movement is weakened, though not completely lost, we speak of *paresis* or *hypokinesis*. Symptoms of motor irritation reveal themselves as *involuntary contractions* and are sometimes described under the designation *hyperkinesis*. Disturbances of coördination are grouped under the general heading of *ataxia*.

### (*a*) *Paralysis, or Palsy, and Paresis*

(*The Akinesias and Hypokinesias*)

Paralytic disturbances of function can be classified in different ways: (1) according to the tonus of the paralyzed muscles; (2) according to the state of nutrition of the paralyzed muscles; (3) according to the distribution of the paralyzed muscles; and (4) according to the gravity of the disease.

Fig. 539.—Organic Hemiplegia of the Right Side on the 5th Day. Note the Exaggerated Passive Flexion of the Fore-arm on the Right. (After J. Babinski, "Gazette des Hôpitaux," published by Bureaux d'abonnement, Paris.)

Fig. 540.—Contracture of Right Upper Extremity, Probably Due to Lesion in, or Near, the Nucleus Lentiformis. (Personal Observation.)

### i. Paralyses Classified According to the Tonus of the Paralyzed Muscles

(*Flaccid and Spastic Paralyses*)

When the tonicity of the muscles paralyzed is less than normal (hypotonic or atonic) we speak of a *flaccid paralysis.* When it is greater than normal, the muscles being rigid (hypertonic), we speak of a *spastic paralysis.* In flaccid paralyses, the deep reflexes are usually diminished, whereas in spastic paralyses they are greatly exaggerated. As a result of paralysis of one group of muscles and hypertony of antagonists, *contractures* are prone to develop.

### ii. Paralyses Classified According to the State of Nutrition of the Muscles Paralyzed

(*Atrophic and Non-atrophic Paralyses*)

While all paralyzed muscles atrophy somewhat from disuse (*atrophy of inactivity*), there are certain paralyses in which a rapid *degenerative atrophy* develops and an electrical reaction of degeneration (see under Electrodiagnosis) appears in the muscles paralyzed. Such *atrophic paralyses* are due to lesions of the lower motor neurons; the *non-atrophic paralyses,* those that show no degenerative atrophy, but only the relatively slight atrophy of disuse without reaction of degeneration, are due to lesions in the motor paths superior to the lower motor neurons. They include paralyses due to lesions of the pyramidal tract and the hysterical or so-called aboulic paralyses.

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### iii. Paralyses Classified According to the Distribution of the Muscles Paralyzed

(*Topography of Paralyses*)

The paralysis may involve: (1) a single muscle or the muscles innervated by a single peripheral nerve (*neural paralysis*); (2) the muscles belonging to the domain of several peripheral nerves and corresponding to the distribution of a plexus or a trunk of a plexus (*plexus paralysis*); (3) the muscles belonging to one nerve root or to one segment (*segmental* or *radicular paralysis*); (4) the muscles of a whole extremity or of a part of an extremity (*monoplegia*); if the face alone be involved, we speak of a monoplegia facialis, if the arm alone, of monoplegia brachialis, if the leg alone, of monoplegia cruralis; or (5) the muscles of several extremities may be paralyzed simultaneously. When the muscles in a pair of extremities (both sides of the face, both arms, both legs) are symmetrically para-

lyzed, we speak of a *paraplegia* or *diplegia;* thus paralysis of both arms is known as paraplegia superior, or paraplegia brachialis; when both legs are paralyzed, it is a paraplegia inferior, or paraplegia cruralis. When the musculature of one-half of the body is paralyzed or paretic, the condition is known as a *hemiplegia.* This may be total, involving face, arm, and leg; or it may be partial, involving only the face and arm, or only the arm and leg of one side. According to the site of the lesion within the central nervous system, we distinguish cerebral from spinal hemiplegias; in the latter, the face is, of course, unaffected. In focal diseases of the midbrain, pons and medulla, there may be a paralysis in the domain of one or more cerebral nerves on one side and of the extremities on the other side, known as *hemiplegia alternans.* According as the lesion involves (1) the N. oculomotorius, (2) the N. facialis and N. abducens, (3) the N. hypoglossus and N. glossopharyngeus, we speak of (1) hemiplegia alternans superior (Weber), (2) hemiplegia alternans inferior (Millard-Dubler), and (3) hemiplegia alternans infima. When the arm on one side and the leg on the other are simultaneously paralyzed we call it a *hemiplegia cruciata* (see also Topical Diagnosis).

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### iv. Paralyses Classified According to the Gravity of the Disease

*(Organic and Functional Paralysis)*

Clinically it is convenient to separate paralyses due to what we call organic lesions of the neuron systems, that is, to changes that are in some

way demonstrable in the tissues by the methods at present at our disposal and largely irreparable, from the so-called functional paralyses, in which no such lesions are demonstrable by the methods we now use, structural changes, if they exist, being so delicate as not to be recognizable by our present means of study. The hysterical and other psychogenic forms come under the head of *functional paralyses,* whereas those due to vascular lesions (hemorrhage, embolism, thrombosis), to tumors, to inflammations and the like are described as *organic paralyses.* The means of distinguishing between these types will be discussed when the diagnosis of the nature of nervous diseases is taken up.

## (*b*) *Phenomena of Motor Irritation; Involuntary Contractions of Striped Muscles*

(*The Hyperkinesias and Parakinesias*)

Through increasing physiological stimuli, through pathological stimuli, or owing to pathological irritability of the motor neuron systems, symptoms of motor irritation (hyperkinesis) may develop.

Such abnormal stimulation or abnormal irritability may affect the lower motor neurons or the upper motor neurons, either (1) directly, or (2) indirectly, (a) through the centripetal conduction paths (reflex hyperkinesis), or (b) through the higher associative conduction paths (psychogenic hyperkinesis).

Among the phenomena of motor irritation manifesting themselves as involuntary contractions of striped muscle, we shall consider (1) fibrillary and fascicular twitchings; (2) tremors; (3) pathological associated movements or synkinesias; (4) chorea and the choreatic disturbances of motility; (5) athetosis and the athetotic disturbances of motility; (6) forced movements, forced attitudes, and conjugate deviations; (7) imperative acts; (8) paroxysms of over-contraction or hyperkinesis (fits or convulsions, cramps, etc.).

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### i. Fibrillary Twitching, Fascicular Twitching and Myokymia

By these movements we mean quick twitchings of single bundles of muscle fibers (*fibrillary twitching*), or of larger groups (*fascicular twitching*), or wavelike fluctuations (*myokymia*) without locomotor effect.

Many persons on exposure to cold present, temporarily, such twitch-

ings or wavelike motions in the larger muscles of the extremities; they may be regarded as the first stages of a rigor or chill. Such contractions, which rarely affect the small muscles of the hand and almost never the muscles of the face, are of no diagnostic significance.

Extremely important for diagnosis, however, are the true fibrillary and fascicular twitchings, which occur in muscles undergoing degenerative atrophy due to lesions in the anterior horns of the spinal cord or in the motor nuclei of the medulla oblongata (progressive muscular atrophy, bulbar paralysis). They appear as brief, intermittent, twitchings in different parts of a given muscle, causing slight visible deformations of the skin. Though usually without locomotor effect, marked fibrillary twitchings in the small muscles of the hand may cause slight movements of the thumb or of the fingers. They are exaggerated by active or passive movements of the muscles involved, or by electrical or mechanical stimulation. The tongue should always be examined for fibrillary twitching, but neurotic individuals often show much twitching in the absence of organic disease; if there be no atrophy of the muscle of the tongue, caution should be observed in deciding that the twitching or tremor is of serious import. Though fibrillary twitchings are most often met with in irritative lesions involving the cell-bodies of the lower motor neurons (anterior horns, motor nuclei of cerebral nerves), they are occasionally seen in diseases of the peripheral motor nerves (neuritis).

Myokymia or wavelike fluctuation is most often seen in the calf-muscles, though it may affect the face, the thigh or other parts. Its cause is unknown, but is probably toxic.

A fibrillation, or myokymia, of the heart-muscle occurs in connection with paralysis of the atria (pulsus irregularis perpetuus) and is recognizable in the electrocardiogram.

### ii. Tremors

By tremors are meant rhythmical, involuntary, to and fro movements of very slight extent; the movements are similar to one another and follow one another in quick succession. They may exist in the absence of voluntary movement, or may appear first on movement.

Normal persons may, during marked excitement, after fatigue, or on exposure to cold, manifest trembling movements of this nature, obvious especially in the handwriting. When a tremor appears without apparent or sufficient physiological cause, it is called a pathological tremor. In certain families, a so-called *essential tremor* occurs, without any symptoms of progressive nervous disease (Dana). It may be local or general.

Tremors may be *fine* or *coarse*, according to the size of the oscillations; and there may be a *rapid* or a *slow* tremor, according to the number of oscillations per second. Fine tremors, like that seen in Graves's disease, are

usually rapid (8 to 12 oscillations per second); coarse tremors, like that seen in Parkinson's disease, are usually slow (2 to 4 oscillations per second), and are sometimes spoken of as "shaking" tremors. They are usually lessened by attempts at voluntary movement, though, occasionally, the reverse is true.

When the tremor appears only on attempts at voluntary movement, or is markedly exaggerated then, it is known as an *intention tremor,* a good example being that seen in multiple sclerosis. In this disease, the tremor is not very rapid; there are usually 4 to 8 oscillations per second (M. Meyer). In the intention tremor of Westphal's pseudosclerosis, there are from 80 to 120 oscillations per minute (v. Strümpell).

A tremor may affect not only the muscles of the extremities, but also those of the neck and trunk, and, sometimes, those of the eyes. In the latter instance, the tremor is known as *nystagmus;* it may be horizontal, vertical or rotary (see Examination of the Vestibular Functions). The remarkable tremor of the lids on gently closing the eyes, so often seen in Graves's disease and in psychoneurotic states, is known as *Rosenbach's phenomenon.*

Tremors, when marked, can scarcely escape observation on inspection. Fine tremors in the fingers may first become visible when one asks the patient to thrust the whole upper extremity straight out from the shoulder, to spread the fingers apart, and to hold the hand stiff between the examiner and the light. Fine tremors can also be sometimes palpated, especially in alcoholics; the examiner asks the patient to rest the tips of his fingers perpendicularly on the palm of his (the examiner's) hand, when very slight jarring or crepitation will be felt (*Quinquaud's phenomenon*). This is present in most alcoholics and may occasionally occur with normal persons.

In *testing for intention tremor* the patient may be asked to touch the end of the examiner's finger or to touch the end of his own nose. The tremor becomes ever more exaggerated as the goal is approached.

To recognize nystagmus one inspects the patient's eyes, first when he is looking straight forward, and afterward when his eyes are directed (a) to each side, (b) upward, (c) downward, and (d) toward the middle line (convergence). A slight nystagmoid movement on strong lateral flexion of the eyes should not be regarded as abnormal, but any oscillation on looking straight forward is pathological.

Tremors sometimes affect one-half of the body and not the other (*hemitremor*), especially in cerebral lesions. When the hemitremor takes the character of marked shaking, it is called *hemiballismus* (Kussmaul), a condition transitional between tremor and hemichorea. Tremors can be recorded graphically, if desired, but the curves reveal nothing of importance inaccessible to the naked eye. Most tremors cease during sleep.

The *cause of tremor* is not well understood, but it is probably related

to disturbances of the tonus-innervations in muscles of reciprocal function (agonists and antagonists). Most tremors, if not all, have a central origin. *Posthemiplegic tremors* are common; that accompanying Benedict's syndrome (paralysis of oculomotor nerve with contralateral hemiparesis and tremor of the paretic extremities) is due to a lesion in the cerebral peduncle.

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### iii. Pathological Associated Movements or Synkinesias[1]

In early life, as the pyramidal tract develops, and later, as skill of different sorts is acquired, the gross mass-movements of the extremities gradually become "dissociated" into "isolated" finer movements, but the tendency to "association" is always there. Skill in performing finer movements consists largely in the voluntary suppression of associated movements. Think, for example, of the degree of isolation of finger-movements in the piano-playing of a Paderewski! Certain associated movements are normally retained throughout life; thus in turning the fingers into the palm to "make a fist," there is always a simultaneous extension (or dorsal-flexion) of the wrist, and on brisk walking, there is always some abduction and some swinging of the arm forward and backward. In certain diseased states, such normal synkinesias may disappear (*e. g.,* in Parkinson's disease and in some cases of hemiplegia).

More common than loss of normal synkinesias are the pathological associations of movement, which appear in diseases of the central nervous system. By a pathological associated movement, is meant one that does not appear in association with a given voluntary movement in a normal person, but that does appear therewith, and cannot be suppressed, in the diseased person.

Pathological synkinesias may be *contralateral,* as in the so-called "identical" synkinesias; *homolateral,* as in the case of the tibial phenomenon of Strümpell, and of the trunk-hip flexion synergism of Babinski; or *bilateral* and general, as in those remarkable cases described as "double athetosis," and in the flexion of all four extremities on passive overflexion of the neck in meningitis (Brudzynski's sign).

**Contralateral Synkinesias.**—In the paralyzed muscles or paretic muscles in a hemiplegic patient, it is not uncommon to see symmetrical contractions appear when movements are voluntarily performed on the opposite (healthy) side of the body; thus, on closing the fist on the non-paralyzed side, the fist of the paralyzed hand may also be closed. Again, but less frequently, attempts to move the muscles on the paralyzed side may result in involuntary symmetrical movements on the healthy side

[1] In the German literature these are referred to as *Mitbewegungen;* in the French literature as *Mouvements associés.*

(*substitution-movements of Senator*). These "identical" synkinesias are seen especially in the movements of the smaller joints; it is as though the movements of the two sides were fused into a unit. Occasionally, movements in a paralyzed arm will appear on voluntary effort to lift the leg of the same side, or contractions in a paralyzed lower extremity may appear on flexion of the arm, or on speaking. On yawning, some healthy people simultaneously extend the upper limbs (*pandiculation*). Such extension-movements may be especially marked in paralyzed limbs during yawning, or as a reaction to tickling. They are especially common in the severer lesions of the pyramidal tract, notably in the infantile hemiplegias.

**Homolateral Synkinesias.**—Some of these are of aid in the diagnosis of lesions of the pyramidal tract.

The Tibial Phenomenon of von Strümpell.—The patient lies quietly in bed on his back. The examiner stands beside him, one hand resting lightly on the thigh of the patient, the other hand laid lightly over the dorsum of the foot of the extremity under examination. The patient is then asked to draw his thigh up toward his trunk by forcible flexion at the hip. In spastic paralysis (upper motor neuron lesion), this leads to an insuppressible contraction of the M. tibialis anticus, visible and palpable, causing dorsal flexion of the foot, which becomes even more marked if the examiner oppose the movement by pressing on the patient's thigh. The M. extensor hallucis longus may also participate in this synergism. The tibial phenomenon may appear on walking, causing the foot to assume an outspoken valgus-position (Oppenheim).

The tibial phenomenon does not occur in every case of pyramidal-tract lesion; it may occasionally be met with when the pyramidal tract is normal. It is, however, a valuable corroborative sign.

The Radial Phenomenon of von Strümpell.—Powerful contraction of the fingers in the making of a fist causes insuppressible excessive dorsal flexion of the hand. This is an exaggeration of the normal associated movement, which can be voluntarily suppressed.

On attempts to lift the arm, hanging supine, an insuppressible pronation also occurs (pronation-phenomenon).

**Bilateral Synkinesias.**—The Trunk-hip Flexion Synergism.—Another associated movement met with in spastic states, first observed by Oppenheim (1889), and given a diagnostic value by Babinski (1900), is an insuppressible flexion of the hip on the trunk on raising the upper part of the body from the dorsal recumbent position. We place the patient flat on his back, without a pillow, on the floor or on a firm mattress, and ask him to cross his arms in front and to keep the legs a little apart. If he now try to sit up without using his arms, the paretic lower extremity will become flexed at the hip and the whole extremity will be raised from the floor, the heel being lifted for a moment, to fall back again later. The shoulder on the healthy side will be carried forward, as if to balance the

weight of the opposite leg. The healthy extremity will remain, throughout its whole length, in contact with the floor. This sign is useful in distinguishing organic from hysterical hemiplegia.

The Synkinesias Involved in Separate and Simultaneous Raising of the Legs (*Phenomenon of Grasset and Gaussel*).—Place the patient flat on his back on the floor, with his arms crossed in front and the legs separated. In incomplete organic hemiplegia, the two lower limbs cannot simultaneously be raised, though either limb separately can be lifted. In hysteria, both legs can be raised at once.

This disturbance of synergism may be shown in another way, by asking the patient to lift the paralyzed limb and hold it in the air. If the healthy limb be now passively raised, the paralyzed limb at once falls, ow-

Fig. 541.—Left-sided Organic Hemiplegia After a Year. Combined Flexion of the Thigh and Trunk on the Left. (After J. Babinski, "Gazette des Hôpitaux," published by Bureaux d' abonnement, Paris.)

ing to the patient's inability to fix the pelvis by means of the muscles on the paralyzed side; but if the patient be asked to raise his healthy leg and we subsequently lift the paralyzed limb passively, the healthy limb will still remain lifted, as the patient can fix his pelvis by the non-paralyzed muscles of the healthy side.

Hoover's Sign for the Detection of Malingering and Functional Paralysis of the Lower Extremities.—This test depends upon the same principles as the two preceding ones, and in practice will be found a very valuable procedure. It is described by my colleague, Prof. H. M. Thomas, as follows:

"Hoover has shown that, when a normal person lying on his back endeavors to lift the extended leg from the couch, the opposite leg is pressed downward, and that in an organic hemiplegia this same pressure occurs when the patient tries to lift the paralyzed leg. If in such a case

the patient lifts the unparalyzed leg, the downward pressure of the paralyzed leg is proportionate to its remaining strength. If the hemiplegia is due to hysteria the action is different. When the patient raises the non-affected leg, the opposite leg, totally paralyzed for voluntary effort, is pressed strongly into the couch, while, if he be told to endeavor to raise the paralyzed leg, there is no movement on the non-paralyzed side, indicating that no outgoing stimuli have left the cerebral cortex, just as if he were consciously simulating the paralysis. Risien Russell has called attention to a somewhat similar phenomenon occurring in hysteria, but in this case it concerns the lack of relaxation in the antagonistic muscles."

**Other Bilateral Synkinesias,**—These are the most remarkable of the whole group. Two examples may be cited: (a) so-called double athetosis and (b) flexion of the extremities on passive flexion of the neck in meningitis.

(a) So-called Double Athetosis.—Here the most extraordinary generalized (but by no means "identical") associated movements occur. The syndrome might, as Lewandowsky suggests, be designated the "disease of the associated movements." The normal dissociation of movements is almost entirely absent. If the patient try to close one eye, or to speak, his whole face breaks out into wild grimacing movements. Isolated movements of the fingers are no longer possible. On walking, the body is thrown into grotesque contortions, "as though one, having slight spasms, tried to walk over eggs." The movements stop during sleep, and, as a rule, when the patient is quietly at rest in bed, awake; but they start again on the approach of anyone, or on the sound of noises.

(b) Flexion of the Extremities on Passive Flexion of the Neck in Meningitis.—This is one of the now well-known Brudzynski signs in meningitis. If the child's neck be forcibly flexed, so that the chin approaches the sternum, both arms and both legs are simultaneously drawn up. (See Part IV.)

**Congenital and Hereditary Synkinesias.**—In certain families, congenital synkinesia occurs, and not only active movements, but also passive and electrically stimulated movements may occur bilaterally (identical synkinesias). In such patients, movements that are to be performed simultaneously, but differ on the two sides (*e. g.,* piano playing), cannot be learned. Since the identical synkinesias probably depend upon the distribution of each pyramidal act to both anterior horns, it may be that in these congenital cases there is an anatomical anomaly—perhaps an excess in homolateral distribution. The phenomenon may occur for generations in the same family (Damsch, Fragstein, Brissaud and Sicard).

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### iv. Chorea and the Choreatic Disturbances of Motility

In chorea we have to deal sometimes with single muscular contractions, more often with combinations of involuntary and somewhat disarranged contractions, occurring quickly and irregularly, and passing from one part of the body to the other without apparent reason. The movements are not wholly coördinated, though they may often resemble purposeful movements such as those of grasping, defense, expression, occupation. In themselves they are unpurposeful, occurring when the patient intends to be at rest or during efforts at voluntary movements, which they disturb by interruption, inhibition, exaggeration, or other alteration. This remarkable form of motor irritation may cause movements of the limbs, of the face and of the tongue, less often of the trunk and eyes, but sometimes even of the pharynx and of the vocal cords. In some cases the movements are unilateral (hemichorea). They are exaggerated by emotion; sometimes they are momentarily lessened by efforts at voluntary movement; they cease, as a rule, during sleep.

Choreiform movements resemble closely the movements of embarrassment that children sometimes show (motiveless feeling, grasping and playing movements of the extremities, by means of which they try to hide internal excitement), a resemblance that has sometimes led parents and teachers to confuse true chorea with the involuntary movements that children show when they become uncomfortable from sitting still for a long time, or when they are fatigued, or in ill-humor.

**Recognition of Choreiform Movements.**—First, we observe the patient at rest for a short period, and look especially for jerkings of the fingers, quick movements of the hands, sudden kicks of the legs, rapid sighing inspirations and the like. If the symptoms are slight, it is well to ask the patient to hold both hands above the head; slight choreiform movements will then usually appear in a few seconds in the fingers of one or both hands. Afterwards, we ask the patient to perform various movements, and note the intercalation of disturbing involuntary contractions. Speech may be interfered with by choreiform movements of the tongue, sudden contractions of the diaphragm, or by swallowing-movements. The choreic patient is clumsy, may drop a plate out of his hand, have difficulty in eating, writing, dressing and undressing, and the like.

**Finer Analysis of the Choreatic Disturbances of Motility.**—Thanks to the careful clinical studies of neurologists, especially those of Bonhoeffer, and of Foerster (1904), we now know that the motility in chorea may be involved in a whole series of different ways. Not only do (1) the spontaneous movements above described occur; but (2) the muscles are often very weak (chorea paralytica, chorea mollis, limp chorea), the paresis of the muscles affecting especially often the neck, sometimes the extremities, in a topographical distribution wholly unlike that in pyramidal tract lesions; (3) the muscles are often hypotonic or atonic (choreatic atony); (4) the voluntary movements are poorly coördinated, as shown by the loss of the normal attitudes of the head, trunk and limbs, sometimes by an outspoken choreatic ataxia, or a choreatic aphasia; (5) attempts at voluntary movement exhibit a markedly long latent period, a peculiar kind of psychomotor retardation, other movements occurring sometimes before the movement "willed," the latter appearing later, as though by chance; (6) there is an inability to maintain the innervation necessary for the continuance of firm contractions; pressure of the hand soon lets up, the hand cannot be held long in a position of dorsal flexion, and the protruded tongue is quickly drawn in again; (7) and, finally, remarkable associated movements occur, differing from those seen in the hemiplegias, since they change in form and extent in the same person with successive attempts to repeat a given movement, the results suggesting that we have to deal less with involuntary movements indissolubly linked to the voluntary movement than with an overflow of the voluntary innervations into other than the normally associated neuron systems.

**Forms of Choreatic Disturbance.**—These movements, occurring in young people in association with rheumatism, tonsillitis or endocarditis, give rise to the picture known as *Sydenham's chorea.* Similar movements coming on after middle life and growing steadily worse, in association with progressive dementia, are known as *Huntington's hereditary chorea.*

Chorea may also be met with in conditions in which diffuse pathological processes exist in the brain (epilepsy, dementia paralytica, dementia praecox, cerebral atherosclerosis); it has been observed in tabes and in Friedreich's ataxia; still more interesting, from the standpoint of pathogenesis, is its occurrence in certain focal lesions of the cerebrum, especially those involving the brachium conjunctivum, the red nucleus and the thalamus. The term *posthemiplegic* chorea is ill chosen, for (1) complete hemiplegia excludes the possibility of this chorea, and (2) this chorea may occur in the absence of even a hemiparesis. Recent studies by J. Ramsay Hunt point to the globus pallidus as the site of lesions in chorea.

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### v. Athetosis and the Athetotic Disturbances of Motility

The athetoid or athetotic movements (W. A. Hammond) are continuous, involuntary, slow, rhythmical movements, most marked in the fingers and toes. The fingers are slowly spread apart or adducted, or alternately flexed and extended. The movements are exaggerated on voluntary movement, and during excitement. They have a wormlike character, the fingers forming very slow, bizarre movements, the single digits moving neither simultaneously nor in the same direction, some digits being extended while others are flexed. The fingers may be over-extended and spread widely apart when the hand is in a position of extreme flexion. The movements have been compared with those of the tentacles of a polyp. The feet are usually less affected than the hands; the foot, when involved, most often shows plantar flexion and adduction with hyperextension of the great toe. Sometimes the movements involve also, to a slight extent, the more proximal portions of the limbs.

Athetotic movements do not occur in limbs that are completely paralyzed, but only in those that are still more or less subject to the will. They usually cease, though they occasionally persist, during sleep.

The muscles of an athetotic extremity are, in contrast with those of a choreatic extremity, hypertonic. This hypertony is sometimes very

marked, often leading to a kind of intermittent spasm; the arms may be strongly pressed against the chest or markedly rotated, the positions changing during active movements or on excitement (spasmus mobilis). This mobile spasm due to hypertony probably represents a transition to a spastic contracture; it may exist, in some cases, in the absence of athetotic movements (so-called *hemitony* of infantile cerebral palsy). The muscles of an athetotic extremity may show hypertrophy instead of atrophy.

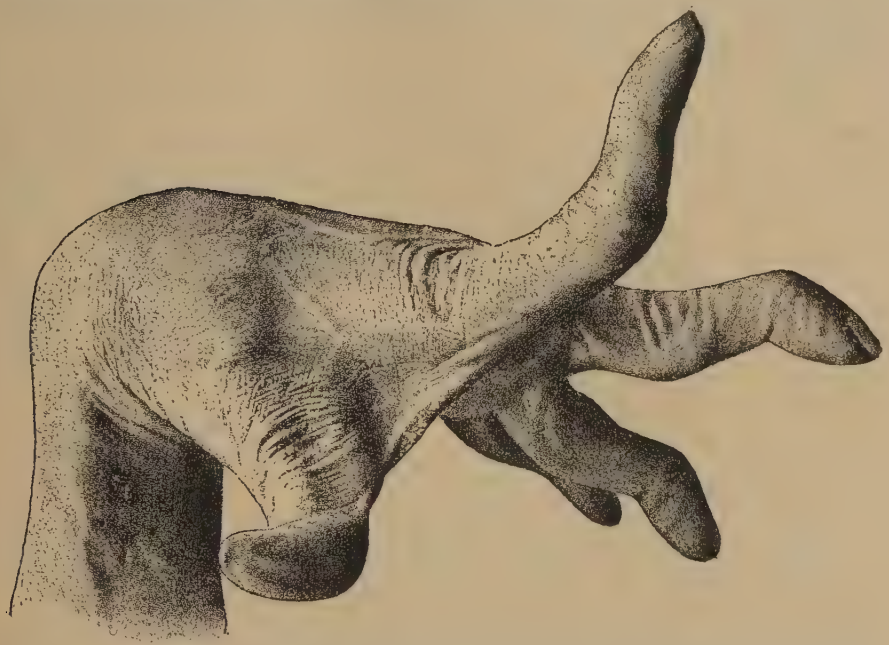

Fig. 542.—Instantaneous Photograph of the Hand in a Case of Posthemiplegic Hemi-athetosis. (After v. Monakow in Mohr and Staehelin, "Handb. d. inner. Med.," published by J. Springer, Berlin.)

**Contrast between Athetosis and Chorea.**—These two conditions are entirely separate and distinct. They may, it is true, occasionally coexist, but each represents a disturbance of motility *sui generis*. The differences are well shown in the following table:

| Chorea | Athetosis |
|---|---|
| 1. Movement begins suddenly; course of movement quick and jerky. | 1. Movements slow and wormlike. |
| 2. When the movement is over, the part remains at rest. | 2. The movements are continuous, ceasing only during sleep; they may be exaggerated or diminished by psychic influences. |
| 3. When at rest, the muscles are relaxed (atonic, hypotonic). | 3. Muscles always hypertonic; transition to spastic states (spasmus mobilis). |
| 4. Movements extremely variable; no trace of rhythmicity. | 4. Movements rhythmical; always the same in the same patient. |

**Causes of Athetosis.**—These are not well understood. Athetosis occurs chiefly in association with diffuse cerebral lesions (encephalitis, porencephaly), acquired in infancy; it is only rarely met with after a cerebral lesion acquired in adult life. Most commonly unilateral, as an accompaniment of infantile hemiplegia, it may be bilateral in cases of infantile cerebral diplegia; this *true bilateral athetosis* has, however, apparently nothing to do with so-called double athetosis (*athétose double*), a disease of the associated movements (*q. v.*), in which athetotic disturbances of motility play a very small rôle, if any.

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### vi. Forced Movements; Forced Attitudes; Conjugate Deviations

Some patients are forced to laugh against their will and in the absence of the corresponding emotion. Such attacks of laughing may be very troublesome to the patient. *Forced laughing* and *forced crying* of this sort are seen in multiple sclerosis and in pseudobulbar paralysis. Many of the crying and coughing attacks of hysterical patients, as well as the phenomena of major hysterical attacks (arching of the back, solicitation movements, forced walking in a circle, etc.), have to be considered here.

In irritation of the right middle cerebral peduncle, or on excitation of the right side of the cerebellum in animals, *forced movements* appear; there is a rotation of the body around its own longitudinal spinal axis in the direction of unscrewing an ordinary screw (the head of the animal corresponding to the head of the screw). But destructive lesions on the right side give free play to the impulses arising on the left side and thus give rise to rotation in the reverse direction; namely, that of screwing in a screw. Besides this forced rotation, we may cite as examples of forced

movements, (1) forced running in a circle, and (2) forced rolling movements. As examples of *forced attitudes,* the forced lateral position, and the crouching position like that of a hunting dog (*en chien de fusil*), sometimes seen in meningitis, may be mentioned; such forced attitudes are often due to painful contractures. Other forced attitudes result from spasm (*e. g.,* in torticollis and in tortipelvis).

*Conjugate deviation of the eyes and of the head* in the same direction (*déviation conjuguée de la tête et des yeux* of Prévost), due either to irritation of agonists or to paralysis of antagonists, is a good example of forced movement. In lesions of the cerebrum causing hemiplegia, the head and eyes often look away from the paralyzed side; that is, toward the side of the lesion in the brain. In rare cases of cerebral irritation, and sometimes in pontile lesions (supranuclear area in region of the fasciculus longitudinalis medialis), the eyes may look away from the lesion, instead of toward it.

Fig. 543.—Patient with Epiphyseal Tumor, Showing Inability to Elevate the Eyes Above the Horizontal. Mobility Lateralward Was Also Slightly Diminished in Both Eyes. (After P. Bailey and S. E. Jelliffe, Arch. Int. Med.)

At least three cortical areas seem to be concerned in combined lateral movements of the eyes: (1) frontal (foot of middle frontal gyrus), (2) parietal (angular gyrus and inferior parietal lobule) and (3) occipital. The fibers from the cortical areas run through the projection-system downward; thus conjugate deviation may follow lesions of the centrum semi-ovale, or of the capsula interna. (For testing for conjugate deviation, see Vestibular Functions.)

In a few cases, the eyes are found turned to one side, and the head to the other (*déviation dissociée*), due probably to paralysis of lateral deflection of the eyes and irritation of the head-rotators.

Often the eyes are alone affected, the two eyes not moving lateralward together

beyond the middle line (*paralysis of lateral associated ocular movements*), but the head being entirely free to rotate in either direction; in such cases the medial recti may work perfectly well for convergence. Such a paralysis always indicates a pons lesion, of the same side (usually in the medial portion of the formatio reticularis headward and ventralward from the nucleus N. abducentis, ventro-lateral from the fasciculus longitudinalis medialis). The fibers from the cortical areas appear to go down to this center and thence return to the eye-muscle nuclei.

Instead of the horizontal combined movements of the eyes, the combined vertical movements may be paralyzed (*paralysis of vertical associated ocular movements*). This is an important localizing symptom, pointing to a focal lesion in the midbrain (superior colliculi of corpora quadrigemina). Spiller, of Philadelphia, has made a careful study of this condition. It may be confused with nuclear paralysis of the eye-muscles; the differentiation is made by diplopia tests.

In some cases of lesion of the lateral lobe of the cerebellum, a *skew deviation* of the eyes has been observed; in a case mentioned by Purves Stewart, the right eye was directed downwards and mediałwards, and the left eye upwards and lateralwards.

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### vii. Imperative Acts; Automatic Habits

In psychasthenic states, patients may be overcome by an irresistible tendency to perform certain acts. Thus some must bite their nails (onychophagia), keeping them always gnawed down to the quick. The tics and the stereotyped movements of dementia praecox are referred to elsewhere.

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### viii. Paroxysms of Over-contraction or Hyperkinesis

(*Fits or Convulsions, Cramps*)

Under this heading we have to deal with the various types of fits or convulsions, cramps, spasms, etc. The terms in use here have never been very sharply defined. As a result, different authors do not always mean

the same thing by the same words. The tendency at present is to limit the word *spasm* to the pathological permanent contractions arising reflexly through purely quantitative increase of physiological stimuli, and to use the term *cramp* to indicate either continuous or intermittent muscular contractions depending on physiological stimuli and on a pathological irritability in the motor neuron systems or perhaps in the muscles themselves.

In the origin of such pathological contractions, summation of stimuli may play a part. In other words, stimulation need not be immediately followed by muscular contraction, but, continuing, leads to a storing up of energy until suddenly a "discharge" takes place. Such motor discharges may lead either to a continuous *tonic* (or tetanic) contraction of the muscles, or to more or less rhythmical, intermittent contractions—the so-called *clonic* contractions. When the contractions are limited to single muscles or small groups of muscles, we speak of *cramps,* but if they involve a whole extremity, or most of the musculature of the body, the term *convulsion* or *fit* is used.

The irritability of great groups of motor neurons is often affected by *toxic* substances circulating in the blood. Some of them have an affinity for the upper motor neurons, others for the lower motor neurons; thus in epilepsy, uremia, eclampsia, etc., it is the upper motor neurons and probably their cell bodies in the cerebral cortex that are chiefly affected, while in tetanus, hydrophobia and strychnin-poisoning it is the lower motor neurons (and probably their cell bodies in the anterior horns of the spinal cord and in the nuclei of origin of the motor cerebral nerves) that are acted upon. In *reflex* convulsions or cramps, the motor discharge is the result of an abnormal increase in centripetal impulses from some local source (reflex contractions as a result of nasal disease, phimosis, intestinal irritation, etc.).

Sudden disturbances of the circulation in the central nervous system can cause motor discharges (*e. g.,* anemic convulsions). Moreover, local inflammation, or trauma, involving the motor neuron systems, may be accompanied by motor explosions (convulsions in dementia paralytica, meningitis, encephalitis, cerebral hemorrhage, thrombosis, etc.).

The more extensive motor fits or convulsive attacks are either cerebral or cerebellar in origin.

### (1) *Cerebral Fits*

The cerebral fits are divisible into two great groups: (1) the psychogenic group of cerebral fits; (2) the epileptiform group. The *psychogenic cerebral fits* include hysterical convulsions and psychasthenic fits.

**Hysterical Attacks.**—The hysterical convulsions consist chiefly of expressive movements, or muscular contractions corresponding to those that accompany strong emotions of various sorts (*e. g.,* anger, erotism, joy,

pain, etc.). During the attack hysterical patients may be influenced by verbal suggestion, and may react to other external influences, such as the behavior of adjacent persons. They do not hurt themselves, as a rule. They may strike those about them. Often the movements reproduce those of some earlier experience (an assault, an accident, a fire). Hysterical catalepsy, hysterical contractures, hysterical chorea, and hysterical myoclonia often give rise to mistakes in diagnosis. A fuller description of hysterical attacks will be found under special diagnosis.

**Psychasthenic Fits.**—Psychasthenic fits may closely resemble epileptic fits; they have been described by Oppenheim, Spiller, Friedmann, and others. They differ from both epileptic attacks and from hysterical attacks. They appear as attacks of unconsciousness, with or without convulsive seizures, often as equivalents of the psychasthenic anxious state. The fits occur in people, who, earlier, have shown anxious states, phobias or tics. They never occur independently of some exciting factor, and are, as a rule, rare incidents in the patient's life. Intelligence and memory are not lessened by the attacks. The condition is not benefited by bromid treatment, but rather by rest-cure methods. In young children, there may be attacks suggestive of petit mal, as many as 6 to 40 a day (Friedmann); these may be related to the "spasmophile diathesis."

**Epileptic and Epileptiform Attacks.**—The epileptic, or the epileptiform, attack may be general, involving the whole body, or local (jacksonian), beginning in a given muscle-group and extending to a smaller, or larger, number of other muscles. The general convulsions include those of *idiopathic epilepsy* (cause unknown) and those of *symptomatic* epilepsy, due (a) to toxic influences, *e. g.*, in uremia, intestinal intoxication, placental intoxication, diabetes, plumbism, alcoholism, (b) to inflammatory, circulatory, or neoplastic changes in the cerebrum itself, *e. g.*, in dementia paralytica, lues cerebri, encephalitis, meningitis, apoplexy, glioma, and (c) to reflex influences, *e. g.*, intestinal worms, scars, nose- and ear-diseases. The local or jacksonian convulsions are due usually to some focal irritation in the cerebral cortex (*e. g.*, tumors, local inflammatory, or circulatory, disturbance).

**The General Epileptic Convulsion** (*Grand Mal Attack*).—These attacks have been carefully studied by a great number of observers, notably by Gowers, by Féré, by Turner, and by Spratling. In true epilepsy, and in epileptiform convulsions generally, there may be a forewarning of the attack in the form of an *aura* (paresthesia in some part, or a sudden sensation of sight, hearing, taste or smell). The patient may or may not cry out at the beginning. He suddenly becomes unconscious, the whole musculature of the body becomes rigid (*tonic phase*), the patient falls to the floor, and the head and eyes are usually rotated slowly toward one side. The extended arms are pressed closely against the body, the forearms pronated, the hands flexed and clenched with the thumbs turned in, the

legs extended. The face, at first pale, soon becomes dark blue, owing to spasm of the respiratory muscles. The pupils are widely dilated and do not react to light. The tonic contractions continue for a few seconds only (rarely for minutes), soon giving way to clonic contractions (*clonic phase*) with violent jerking of the extremities, the jerkings being slight, at first, but growing gradually more violent and involving not only the muscles of the extremities, but also those of the face, eyes and tongue. The violent clonic spasms of the jaw-muscles often result in biting of the tongue and bleeding. The patient may pass urine or feces involuntarily. The clonic contractions last for a few minutes ($\frac{1}{2}$-5 minutes) only, and then gradually die down. The patient may open his eyes for a moment but remains for a time in *coma*, which, in turn, is often followed by a deep sleep, lasting from a half to several hours. If he be artificially aroused, he may exhibit a twilight-state, behaving automatically for a time. On awaking spontaneously, the patient complains of fatigue and headache. He may be slightly confused; he has no memory of the attack (*amnesia*). During the attack, the temperature rises slightly (not more than 0.5° C.), the corneal and pupillary reflexes are abolished, sometimes the tendon reflexes also. Babinski's sign may be positive. Such an attack is known as major epilepsy (*grand mal*). Rudimentary attacks, in which there may be no convulsion whatever, but simply a momentary unconsciousness, without aura or post-epileptic coma, are known as minor epilepsy (*petit mal*). Sometimes peculiar mental states with abnormal behavior (ambulatory automatism, fugues, poriomania) occur as psychic *equivalents of epileptic attacks* (see Special Diagnosis).

**Jacksonian Attacks** (Cortical Epilepsy).—In this form of convulsion, the abnormal contractions begin in a definite group of muscles, and extend gradually to others, or to the whole body. They may not be associated with loss of consciousness. The convulsion may be confined to one extremity, or to one half of the body. It usually begins in a localized group of muscles (a single muscle, or a group variable in size) of the face, hand or foot, and extends gradually, in the form of a "march," to other muscles of the same extremity, and then to the rest of the body. Along with the involvement of the whole musculature on one side of the body, there is usually conjugate deviation of the eyes and of the head to the opposite side.

The *order of the march* depends (1) upon the situation of the primary focus of irritation in, over, or beneath the cortex, and (2) upon the localization of movements in the central gyri. Thus contractions beginning in the face extend to the arm and then to the leg. Those beginning in the leg extend first to the arm and then to the face. Those beginning in one arm extend, as might be expected from what we know of cortical representation of movements, approximately simultaneously to face and leg. The convulsive movements, in passing from one side of the body to

the other, go first to the leg, then to the arm, and, lastly, to the head. The march may be arrested at any point without further involvement of the musculature. Unilateral attacks, frequently recurring, are known as *status hemi-epilepticus.*

The muscles in which the movements begin are often paretic after the attack is over. The contractions are usually clonic at the beginning of the attack; these quickly become accentuated, and lead into a tonic phase, which lasts a few seconds, after which the contractions are again clonic in type. There are, however, great variations; in some cases there is no tonic phase; in others the whole attack is tonic. The convulsion may last a few minutes, several hours, or even for days. During the attack, the conscious patient, as on electrical stimulation of the cortex (Cushing), has no motor idea corresponding to the movement; he is surprised to see and feel the contractions of the muscles. Strong attempts to overcome the beginning contractions (resistance to the movements made with the opposite arm or leg) will sometimes arrest an attack (Gowers).

Jacksonian, or cortical, epilepsy is usually a sign of circumscribed irritation in the brain (*e. g.,* trauma, tumor, abscess, gumma, tubercle, local meningitis, vascular lesion, scar), but similar circumscribed epileptiform convulsions are occasionally observed in diffuse irritations (*e. g.,* increased intracranial pressure), in toxic states and in "genuine" epilepsy.

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[Note.—See also references under Epilepsy.]

### (*2*) *Cerebellar Fits*

The forced movements, so typical in animals, are rarely seen in cerebellar disease in man, though Ballance has observed them after operations on the cerebellum. A forced "cerebellar attitude" of the head (the ear tilted toward the shoulder on the side opposite the tumor and the face

turned slightly toward the side of the lesion) has been reported by Batten in lateral-lobe lesions.

Two main types of cerebellar fits have been described, though it is not yet quite certain whether they depend upon irritation of motor structures or of centripetal paths in the neighborhood. Several possibilities have been suggested: (1) path from cerebellum to Deiter's nucleus to spinal cord; (2) path from cerebellum through brachium conjunctivum, (a) to red nucleus, Monakow's bundle and spinal cord, or (b) to thalamus, cerebral cortex, pyramidal tract and spinal cord.

**Cerebellar Fits, Supposedly Due to Unilateral Lesion.**—The contractions are tonic, not clonic, and are more marked in the homolateral limbs than in those of the opposite side. The arm and leg on the side chiefly affected are firmly adducted; the contra-lateral limbs are abducted; the head, neck and trunk, as well as the limbs, undergo a screwlike rotation from the side of the lesion toward the healthy side (Stewart and Holmes), and there is conjugate deviation of the eyes toward the healthy side.

**Cerebellar Fits Supposedly Due to Irritation of the Vermis.**—The contractions are tonic, not clonic, and consist of retraction of the head with arching of the back (opisthotonos), supination of the hands and flexion of the elbows; the legs are rigidly extended with the toes pointed (Hughlings Jackson).

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### *(3) Pure Tonic Spasms*

In some motor paroxysms the contractions are all tonic in nature.

**Tetanus.**—In tetanus there is general hypertony, and under the influence of slight sensory stimuli (tactile, acoustic, optic) tetanic attacks are precipitated. The face becomes rigid, often in the form of a sardonic grin (*risus sardonicus*); the patient grits his teeth and holds the jaws firmly closed (*trismus* or *lock-jaw*); the head bores into the pillow; the back may be arched so that the body is supported by the back of the head and the heels (*opisthotonus*); respiration may be interfered with by fixation of the thorax in full inspiration; the abdominal muscles are tense and the abdominal wall retracted; the arms and legs are held rigidly extended.

**Hydrophobia.**—Here the tonic spasm affects especially the muscles of deglutition (so-called cephalic tetanus). A loud noise, a bright light, or any other stimulus, may induce the spasm, though it is especially the attempt to swallow liquids that calls it forth (hence the term hydrophobia).

**Strychnin Poisoning.**—Paroxysms similar to those of tetanus occur in poisoning by strychnin. They differ from tetanus in two important respects: (1) they begin with clonic contractions, which quickly become tonic; (2) between single paroxysms there is complete muscular relaxation, and not simply, as in tetanus, a remission in the degree of contraction.

**Tetany.**—The tonic spasm in tetany (due to parathyroid insufficiency) affects chiefly the musculature of the distal portions of the extremities. The contractions are bilateral and symmetrical and are usually painful. The hand assumes the "obstetrical position" (conical shape, fingers extended at interphalangeal joints, slightly flexed at metacarpophalangeal joints, all digits pressed together with thumb tucked inside fingers, hollow of palm deepened from contraction of muscles of thenar and hypothenar eminences). The contractions in the legs are also characteristic (ankle dorsiflexed, foot slightly inverted, toes strongly flexed). Pressure on nerve trunk in sulcus bicipitalis, produced either by the fingers, or, better, by the band of a blood pressure apparatus, calls forth a cramp (Trousseau's phenomenon) resembling that occurring spontaneously.

### (4) *Motor Tics and Habit Spasms*

By a tic is meant a reflex movement, an expressive movement, or a defensive movement that has become an imperative movement. It occurs as a result, not of an external stimulus, nor of an adequate psychic process, but as the result of a pathological irresistible impulse to movement. The kinesthetic memory is excessively lively in consciousness, with resulting necessity of performing the movement. Patients are able temporarily to resist the impulse, though this resistance is associated with marked discomfort, and, sooner or later, relief is sought by resorting to the act. A tic is characterized by (1) a somewhat shorter and more violent movement than the corresponding normal movement, and (2) the fact that the movement is frequently repeated. A tic may be *local,* involving a single muscle or a small group of muscles, or *general,* involving most of the muscles of the body (*maladie des tics impulsifs, q. v.;* myospasia impulsiva).

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### (5) *Localized Muscle Cramps*

These are divisible into two groups: (a) those due to direct irritation of lower motor neurons, and (b) those of reflex origin.

(*a*) *Cramps or Spasms Due to Direct Irritation of Lower Motor Neurons.*—While the tics above mentioned affect, as a rule, complicated movements corresponding to certain acts in which muscles of different innervation participate (sucking, snuffing, licking, biting, snarling, scratching, plucking, gritting, clucking, etc.), there are many cramps due to irritation (nuclear or infranuclear) of lower groups of neurons, often limited to the domain of single muscles or nerves. In contrast with tics, these spasms may occur during sleep. Among them may be mentioned the various forms of facial spasm, glossospasm, pharyngismus, some forms of torticollis, respiratory spasm (including some cases of hiccough or singultus) and cramps in the calf-muscles (due to metabolic disturbances).

(*b*) *Local Reflex Cramps.*—As examples may be cited (1) the rigidity of the neck in meningitis; (2) reflex facial spasm in tic douloureux; (3) the cough in pertussis and other reflex coughs, and (4) saltatory reflex cramp in the lower extremities, causing hopping or dancing movements when the feet touch the floor, though it may be that this is hysterical in nature.

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### (6) *Myoclonia*

Here also should be mentioned an affection characterized by clonic contractions, involving chiefly the muscles of the extremities and of the trunk, the face usually escaping. These contractions are brief and lightninglike; they usually cease during sleep, are arrhythmical, affect muscles independent of synergism, and may at times be confined to a single muscle that cannot be independently innervated by the will (M. brachioradialis). Indeed, this muscle, the M. biceps, the M. trapezius, the M. quadriceps and the M. semitendinosus are those most frequently involved. Myoclonic contractions are sharply to be distinguished from fibrillary twitchings. The condition was described by Friedreich as *paramyoclonus multiplex;* in his case the face was unaffected. Schultze de-

scribes cases in which the face alone was involved as *monoclonia*, designating the Friedreich cases as *polyclonias*. Some of the cases that have been called chorea electrica were probably instances of myoclonia. The occurrence of myoclonia in certain types of epilepsy and of dementia will be referred to under Special Diagnosis.

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[Note.—For other references, see Part XII, Section III, Special Diagnosis of Myoclonia.]

## (7) *Occupation Cramps*

Some persons manifest cramps involving movements that pertain to their occupations, that is, complicated movements in which skill has been acquired by long practice. Among them may be mentioned writer's cramp, piano-player's cramp, seamstress's cramp, telegrapher's cramp, shoemaker's cramp and cigarette-roller's cramp.

These occupation neuroses usually occur in psychopathic persons, especially on fatigue or under the inhibiting effect of strong emotion (expectation, anxiety, fear of losing one's place, etc.). When the cramp exists, the more one tries, the more marked it is, while a "don't-care attitude" will sometimes overcome it.

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## 7. Phenomena of Incoördination

(*The Ataxias and the Abnormal Gaits*)

Under this heading we shall consider static coördination and locomotor coördination and their disturbances.

### (*a*) *The Ataxias*

By ataxia is meant disordered or incoördinated movement. The patient, on making movements, betrays his uncertainty; he may fail to attain the goal of the movement, erring in direction, in distance, in smoothness, and in velocity (*dynamic ataxia*). He may not be able to maintain an extremity, or his trunk, in a quiet position when muscular contractions are necessary to overcome the force of gravity (*static ataxia*). The gross strength of the muscles may be entirely retained in ataxia; though ataxia may coexist with motor weakness, in which event the movement will be paretic-ataxic, and in hypertonic states, spastic-ataxic, either of which conditions may be met with in the so-called ataxic paraplegia of Gowers.

In testing the coördination of muscles we have learned that, in every purposeful movement, there is a complicated play of the muscles that act together (synergists). Not only do the prime movers (so-called agonists or protagonists) contract, but also accessory muscles, which help the main contraction or fix portions of a limb during contraction, and often the muscles directly opposite in effect (antagonists) to the protagonists, are either relaxed through inhibition of their tonus, or contracted in varying degrees to make the movement steady, precise and certain. The excitation of the protagonists and the inhibition of the antagonists depend upon impulses coming from neuron systems in the brain and spinal cord lying superior to the lower motor neurons, above all from the pyramidal tract.

But the degree of contraction and relaxation of the different groups of muscles concerned in a given movement is constantly varying during the movement itself, and these variations depend in large part upon the centripetal impulses received by the central system during the performance of the movement. Only a part of these centripetal impulses have a conscious correlate (joint sense, sense of muscular contraction, sense of innervation, etc.). The majority of these centripetal impulses, in all probability, are subconscious or unconscious, and pass (1) by the reflex collaterals in the posterior roots to the anterior horn cells, (2) through the direct cerebellar tract and Gowers's tract to the vermis of the cerebellum and (3) through the posterior funiculi and the corpora restiformia to the cerebellum. The cerebellum is in turn connected by its superior peduncles (brachia conjunctiva and the decussation of the latter), with the red nucleus, and, ultimately, with the cerebral cortex. This connection permits of the passage of impulses in both directions—from cerebellum to cerebrum, and from cerebrum to cerebellum. The cerebellum is also thrown under the influence of the cerebral cortex by impulses that go by collaterals from the pyramidal tracts to the nuclei pontis, and thence through the middle cerebellar peduncles (brachia pontis) to the lateral lobes of the cerebellum, there to end about the Purkinje cells. Both the red nucleus and the cerebellum are in turn directly and indirectly connected with the gray matter of

the spinal cord by spinopetal paths. These great systems of neurons must be regarded as the principal coördinating mechanisms. For the maintenance of equilibrium, the vestibular paths and the centripetal paths from the eye-muscles and from the muscles of the head and the joints of the spine, both of which are connected with the cerebellum, are probably of prime importance. Finally, the optic paths are of considerable importance in locomotor coördination, and the acoustic paths are of especial importance in the coördination of the complicated speech-movements.

One sees how large a part of the central and peripheral nervous systems can be concerned in the coördination of movements. Since disease of any of the parts mentioned may cause incoördination, it is obvious that the unravelling of the pathogenesis of an ataxia may be a difficult problem. Certain clinical types of disturbance of coördination present themselves frequently. It is customary to distinguish static ataxia or incoördination from dynamic or locomotor ataxia or incoördination.

When there is loss of ability to hold an extremity at rest in an elevated position (opposing the force of gravity), or to maintain the body as a whole in the upright position (sitting or standing), *static ataxia* is said to exist.

When the disturbance of coördination is noticeable on the performance of a movement, especially in making changes of position of the extremities, or the carrying out of purposeful movements of various sorts, the condition is called *dynamic* or *locomotor ataxia.*

As has been said, there may be no diminution of strength in the muscles concerned, and when paresis of the muscles coexists (as in cerebral ataxia and in ataxic paraplegia), it is to be regarded as a separate disturbance. While disturbance of the deep sensibility (of the joints, muscles, tendons, etc.) is often present (especially in the tabetic type of ataxia), it will be easily understood, from what has been said above, that in many cases of ataxia (especially cerebellar ataxia) no disturbance of such sensibility may be demonstrable. Much more frequent than the association of anesthesia is that of hypotony with ataxia.

Four distinct types of ataxia are distinguishable: (1) peripheral and spinal ataxia due to loss of centripetal (conscious and infraconscious) impulses from the bones, muscles and joints; (2) vestibular ataxia due to lesions of the labyrinth or of the N. vestibuli or its intracentral continuations; (3) cerebellar ataxia, and (4) cerebral ataxia.

### i. Peripheral, Radicular and Spinal Ataxia, Due to Loss of Centripetal Impulses

The commonest example is the locomotor ataxia seen in about one-third of the cases of tabes. It is due less to a loss of conscious sensations (bathyanesthesia), though these may be in part concerned, than to a loss of unconscious centripetal regulating influences, which pass from the muscles, bones and joints along the afferent peripheral nerves, the pos-

terior roots of the spinal nerves, and through the afferent paths in the cord to (1) the anterior horns, and (2) higher regulatory neuron systems. Usually there is demonstrable bathyanesthesia and loss of the deep reflexes, but there may often be a high grade of ataxia with very slight objective sensory disturbance. Undoubtedly, the associated hypotony (Frenkel) of the muscles is of importance; movements performed by the muscle-groups that are most markedly hypotonic, are the most ataxic. As we have emphasized when considering muscle-tonus, what is called tonus is now thought to be synonymous with coördinated contractions of muscles when a part is at rest.

On finer analysis of the ataxic movements, one may (1) describe the effects that the faulty action of each single group of muscles can have in all movements that can occur (O. Foerster), or (2) limit the description to the functional disturbances that occur on performing certain only of the coördinated acts (lying down, standing up, walking, rising from, and sitting down upon, a chair, ascending and descending stairs, special movements of the extremities, face, vocal cords and eyes) (M. Lewandowsky).

Besides tabes (lesions of sensory roots), the peripheral type of ataxia may be seen in polyneuritis, and in pellagra. The similar ataxia in the ataxic paraplegias (pernicious anemia, etc.) is due to the toxic degeneration of the centripetal paths in the spinal cord.

### ii. Vestibular Ataxia

The vestibular and vestibulo-cerebellar incoördination has been described under the vestibular senses and their anomalies (*q. v.*).

### iii. Cerebellar Ataxia

It is very difficult sharply to separate cerebellar ataxia from vestibular ataxia. The labyrinth exerts its influence largely through the cerebellum; the cerebellum, in turn, depends, for the exercise of its functions, in no small measure, upon the centripetal vestibular impulses.

The striking features of cerebellar ataxia are (1) difficulty in standing upright, and (2) difficulty in walking.

The patient, if he can stand at all, does so with his feet spread widely apart—with a "broad base"—swaying from side to side. The visual sense helps the cerebellar ataxic less than the tabetic ataxic, though Romberg's symptom is positive in some cases.

The *gait* is that of a drunken man (*démarche d'ivresse*), the patient reeling from side to side (cerebellar titubation), progressing in zig-zag fashion, with strong tendency to fall, sometimes in a definite direction. In unilateral disease, the patient falls toward the side of the lesion; in

bilateral disease, or in lesions of the vermis, he falls usually backward, less often forward.

We try to analyze in each case how much of a cerebellar ataxia is due to disturbance of the power to orient the body in space (vestibular component) and how much to disturbance of the coördination of the muscles dependent upon centripetal impulses from the bones, muscles and joints (as in radicular ataxia).

The latter component and its associated hypotony are always much less marked than in tabetic ataxia, and that present in cerebellar ataxia concerns the movements of the trunk much more than those of the extremities.

Babinski has described in cerebellar cases a peculiar *cerebellar asynergy,* manifest in a tendency of the upper part of the body to remain, on walking, behind the lower extremities; it is as though the "legs were

Fig. 544.—Cerebellar Asynergy. Attitude in Walking; Patient Held by Two Assistants. (After J. Babinski, "Revue Mensuelle de Médecine interne et de Thérapeutique," published by Octave Doin et Fils, Paris.)

Fig. 545.—Attitude of a Healthy Subject on Standing, Trying to Hold His Head Back and to Curve His Back in the Form of an Arc. (After J. Babinski, "Revue Mensuelle de Médecine interne et de Thérapeutique," published by Octave Doin et Fils, Paris.)

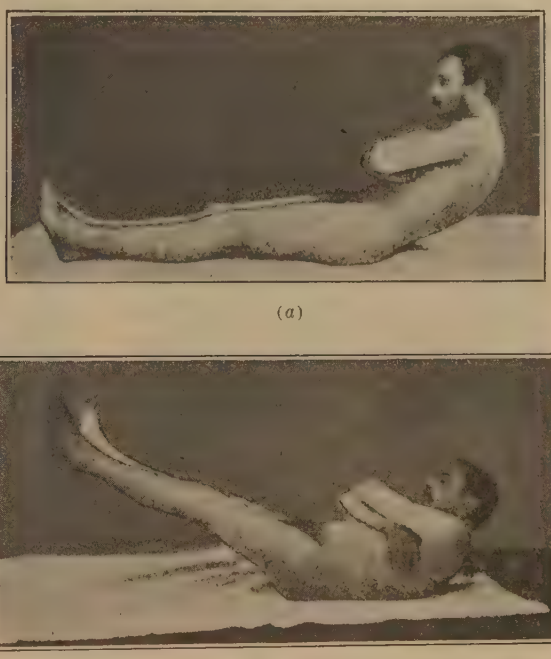
running ahead of the center of gravity." The same patient, on attempting to touch an object with his feet, will make the movements in the knee and hip, not simultaneously, but successively, first in one joint, and then in the other. The hip-trunk flexion synergism (see Pathological Associated Movements) is also demonstrable in such cases.

In how far cerebellar ataxia may depend upon interference with cerebellofugal, rather than cerebellopetal, impulses has not yet been determined.

In cerebellar ataxia, a patient may, lying on his back, be able to hold one or both legs up in the air much more steadily even than a normal man (Babinski). This is a kind of *cataleptoid state,* in marked contrast to the wobbling of the legs (static ataxia) seen in tabetics on making a similar attempt.

Another sign, the discovery of which we owe also to Babinski, is that of *adiadochokinesis.* By this is meant loss of the capacity to make

Fig. 546.—Cerebellar Asynergy. Attitude on Standing; the Patient is Trying to Hold His Head Back and to Curve His Trunk Backwards in an Arc. (After J. Babinski, "Revue Mensuelle de Médecine interne et de Thérapeutique," published by Octave Doin et Fils, Paris.)



(*a*)

(*b*)

Fig. 547.—(*a*) Attitude of a Healthy Subject Trying to Raise Himself from a Recumbent to a Sitting Posture; (*b*) Cerebellar Asynergy. Attitude of Patient Trying to Raise Himself from Recumbent to a Sitting Posture. (After J. Babinski, "Revue Mensuelle de Médecine interne et de Thérapeutique," published by Octave Doin et Fils, Paris.)

opposing movements in quick succession, for example, pronation and supination of the hand lying on the thigh. The rapidity is much lessened on the side of the disease in unilateral cerebellar lesions. The slowness of speech, sometimes seen, may be related.

The diminution of motor strength on the side of the lesion in unilateral cerebellar lesions has been described as *cerebellar hemiplegia*

(Mann); the weakness affects all the muscles, not certain muscles of predilection only as in the cerebral hemiplegias.

The tonic spasms in cerebellar lesions have been described under the hyperkinesias (*q. v.*).

**Occurrence.**—Cerebellar ataxia occurs in a variety of conditions. It is often due to focal lesions (tumor, abscess, hemorrhage, multiple sclerosis, etc.). It occurs sometimes in hydrocephalus, in meningitis serosa and in dementia paralytica. That it may be due simply to a diffuse poisoning is evident from ordinary alcoholic intoxication.

In attempts at localization, it is important to remember that the movement-ataxia, the hypotony, the hemiparesis and the adiadochokinesis

Fig. 548.—Cerebellar Asynergy. Fifteen Seconds Exposure. In This State, Volitional Static Equilibrium May be Maintained in a Perfect Manner. (After J. Babinski, "Revue Neurologique," published by Masson et Cie, Paris.)

Fig. 549.—Tabetic Ataxia. Fifteen Seconds Exposure. Note the Instability of the Legs. (After J. Babinski, "Revue Neurologique," published by Masson et Cie, Paris.)

are, in unilateral lesions, all on the side of the lesion. When the symptoms are equally marked on the two sides of the body, we have to think of lesions of the vermis, or of bilateral lesions of the cerebellar hemispheres or cerebellar conduction paths (see Topical Diagnosis).

### iv. Cerebral Ataxia

Lesions of the lemniscus medialis, anywhere between the decussation in the medulla and the somesthetic area of the cortex can cause a unilateral movement-ataxia with anesthesias, with hypotony, and usually with, but sometimes without, a paresis of the muscles. This ataxia resembles peripheral or radicular ataxia, except that it is unilateral; this is not surprising, since it is due to lesion of the same paths in their cerebral continuations.

The so-called *frontal ataxia* (Bruns), met with in tumors of the frontal lobes, is of the cerebellar type, and is probably, in reality, a cerebellar ataxia, due to "chronic *contrecoup*."

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## (*b*) *The Pathological Gaits*

In normal walking, the body, inclining forward, is at each step shoved forward by extension of the hindward leg. In each lower extremity, the activity is divisible into three periods: (1) that of the swing forward; (2) that of support; and (3) that of the shove of the body forward.

The *period of the swing* begins when the foot leaves the ground, and ends when it touches it again. During it, the hip is flexed, the knee is flexed, the foot dorsally flexed; then the whole extremity swings past its fellow; next the knee is extended, the heel touches the ground; meanwhile the body has been shoved forward by the other leg and would fall, were it not supported at once.

The *period of support* begins at once, the moment the heel touches the ground, and continues until the body is again upright. The knee now becomes slightly flexed.

The *period of shoving the body forward* begins the moment the supporting leg passes beyond the vertical. The "shove" occurs after

extension of the knee and lifting of the heel; the ball of the foot and the toes, the last to leave the ground, give the body a thrust forward.

In walking, the trunk, besides being raised and lowered a little, (4 cm.), inclines at each step slightly lateralward toward the supporting foot. As a leg swings forward, the trunk is slightly rotated, and the opposite arm is (actively) swung.

Normal people vary slightly in their gait, but, in disease, certain very characteristic gaits present themselves for observation. Only the more important of these will here be described, namely, (1) the paretic gait, (2) the spastic gait, (3) the ataxic gait, (4) the reeling or titubating gait, (5) the Parkinsonian gait (propulsion and retropulsion with trepidation) and (6) the "walk with little steps."

(1) **The Paretic or Paralytic Gait.**—The walking is slowed and the steps shortened. The legs are dragged. If the thigh-muscles are weak, the patient leans forward, supporting the arms by canes. When there is a tendency to foot-drop, the leg is lifted high in order to clear the foot from the ground (high-stepping gait; rooster gait). This *steppage* may be met with in polyneuritis, poliomyelitis, and the muscular atrophies.

(2) **Spastic Gait.**—The patients walk with small, hopping steps; the knees are held stiff; the foot shows plantar flexion, and the toes tend to "stick to the floor," wearing out the toes of the boots (spastic paraplegia from cord disease). In organic hemiplegia, the weak leg is held straight and swung forward and lateralward in a curve (scythe movement), since the weakening of the shorteners of the leg and the contracture of the lengtheners (especially of the calf muscles) makes flexion at the knee and elevation of the point of the toe difficult, or impossible. The arm is held flexed, and at every step on the paralyzed side, it is lifted like a wing. In cerebral diplegia, or double hemiplegia, each leg is jerked forward, in turn, with a circular swing; the adductor spasm makes the knees cross alternately in front of each other ("scissors gait").

(3) **Ataxic Gait.**—In the ataxic gait of tabes, polyneuritis, and Friedreich's disease, the legs are slung forward with excess of force, and to irregular distances. They may be lifted high, as in the high-stepping gait, and carried far forward and outward, or only small steps may be made. The patients cannot "walk a crack," and the single steps taken are very uneven. Many of the movements are made too suddenly, or violently, and, when the feet return to the ground, they come down forcibly, flaillike, the heels stamping the floor. The incoördination is much increased when the eyes are closed. Sudden turning and walking backwards are not possible. When the eyes are open, the patient watches the floor and his feet closely, as a help in guiding his movements.

In the ataxic gait, the hip is flexed too much during the period of the swing, and as it passes its fellow it is (owing to hypotony) over-extended at the knee. The patient cannot properly grade his innervations; since under-innervation would

not raise the foot sufficiently, he attempts correction by over-innervation. The foot may, during the swing, be held in an abnormal position (toe-drop; deflection to one side). During the third period, that of the "shove forward," he does not properly lift the heel from the ground. This lifting of the heel should begin almost at the moment the foot comes to the ground after the swing; the ataxic allows the heel and the sole to remain on the ground, so that the body, instead of being lifted forward, is thrown backward, and the patient may fall on his back. Owing, too, to insufficient innervation of the M. gluteus medius and the Mm. peronei, the pelvis sinks toward the side of the supporting leg; thus the body is bent inward, unless the patient prevents it by quickly placing the swinging leg in an abducted position, or by keeping the pelvis raised with a cane on the side of the supporting leg.

The ataxic, during the "period of support," as the extremity approaches the vertical, extends the knee fully, while, as we have seen, normally, the knee is slightly flexed, permitting of an elasticity and evenness of gait otherwise unattainable. In the ataxic, the knee may even be over-extended, as in genu recurvatum.

(4) **The Reeling, Titubating or Drunken Gait.**—This is the gait of so-called cerebellar ataxia. The patient walks as though he were tipsy, making great oscillations from side to side. He stands uncertainly, walks with a very broad base, and, usually, only with support. In this staggering and lurching, the feet are not lifted high, nor are they stamped down as in tabes. There may be a tendency to fall to one side, or forward, or backward. The peculiar relation of the trunk to the legs, sometimes seen, has been mentioned above (cerebellar asynergy of Babinski). Many of these patients are dizzy.

(5) **The Parkinsonian Gait.**—The patients hold themselves stiff and walk with short shuffling steps, which tend to get faster and faster (festinating) as they go forward, "chasing their center of gravity" (*propulsion*). If, when standing, a patient be pulled gently from behind, he tends to run backwards with short quick steps, often falling unless caught (*retropulsion*). The arms are not swung as the patient walks. These features, combined with the expressionless face (*Parkinsonian mask*), the stoop, the flexed arms and the pill-rolling tremor, make a very characteristic picture, once seen, never to be mistaken.

(6) **Walking with Very Short Steps.**—Now and then, on the street, one sees an elderly man making slow progress by means of very short steps. This is the well-known *démarche à petits pas* of French writers. Marie regards it as an important sign for the diagnosis of his "lacunar disease" of the cerebrum, a condition in which, at autopsy, the small arteries of the brain show visible perivascular spaces or lacunae.

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## 8. Disturbances of the Higher Motor Functions

These include (1) the dysarthrias, the motor aphasias and the agraphias; (2) the apraxic disturbances; (3) the disturbances of the expressive movements; and (4) the disturbances in the domain of conduct or behavior (will).

They will, for the sake of systematic completeness, be referred to here, but only briefly, and will be dealt with at greater length in other sections.

### (*a*) *Disturbances of Coördination of the Movements of Speech and Writing*

(*Dysarthria, Motor Aphasia, Agraphia*)

The capacity for speech depends upon the power to perform the movements necessary for the pronunciation of the sounds of the vowels and consonants. When the loss of the power is not due (1) to a change in the general mental state (as in the psychoses, or in hysteria), or (2) to lesions in the muscles, the lower motor neurons, the pyramidal tracts (paretic or spastic states), or to ataxia, any of which may cause *anarthria* or *dysarthria,* the condition is called *aphasia.* The inability may be complete or partial; in the latter case the involvement of spontaneous speech, of the power to repeat words, or series of words, heard, of the power to understand what is heard, of the power of reading, writing, calculating, etc., may vary greatly with the single case. Inability to write is called *agraphia.* The methods of examination are given further on.

### (*b*) *The Apraxic Disturbances*

The inability to make use of the extremities for certain definite combinations of movements, necessary for the performance of certain acts, though there is no paralysis of the muscles, is known as *apraxia.*

These disturbances, including the motor and the ideatory forms, are also considered further on.

### (*c*) *Disturbances of the Expressive Movements*

The expressive movements include the *mimic, pantomimic* and *gesticulatory* movements. They are movements especially associated with affective states—the feelings and the emotions—and depend upon the intensity and the quality of these. The facial movements of laughing and of crying, of pleasure and disgust, come under this heading. The forced laughing and crying of multiple bilateral cerebral lesions (pseudobulbar paralysis, multiple sclerosis, cerebral softenings) have already been referred to. (See Forced Movements). Most remarkable alterations in these expressive movements are seen in mania and in melancholia. They are exaggerated in the former and diminished in the latter (apathy, stupor). An excessive tendency to grimaces and gesticulation is sometimes seen in dementia praecox.

Loss of the expressive movements on one side may occur with contralateral lesions of the thalamus.

### (*d*) *Disturbances in the Domain of Conduct and Behavior* (*Will*)

Any discussion of the efferent or centrifugally-conducting neuron-systems would be incomplete without at least mention of those spontaneous movements of persons that make up their conduct and behavior. It is in these that the normal variations in human beings are chiefly expressed, and there are great deviations within the limits of what we call normal. It is only when conduct diverges very markedly from the average that we dare speak of it as pathological. A study of abnormal conduct belongs to the domain especially of psychiatry.

When the spontaneous movements of a person are greatly exaggerated, we speak of *motor agitation,* and when greatly diminished, of *aboulia* and of *motor stupor. Maniacal excitation* is an example of the former, and the *psychomotor retardation of melancholia* of the latter. In mental disease we often see *stereotyped attitudes* long maintained, the head, for example, being held in an abnormal position for a long time. In dementia praecox, such stereotyped attitudes—attitudes that would be most uncomfortable for a normal person—are maintained for hours at a time and the patients resist any interference with them (*negativism*), or they may monotonously repeat various movements, simple or complex (*stereotyped movements*). Among these may be mentioned snoutlike projection of the lips, swaying movements of the head and trunk, and

tattoo-movements of the arms. Sometimes the patients repeat nonsensical words over and over again (*verbigeration*), or they talk rapidly and continuously (*logorrhea*), or confusedly, in unintelligible sentences, mixed up with rhymes and alliterations (*speech-confusion, word-salad*).

Monotonous renewal and repetition of a movement, either following on a single spontaneous movement, or on a single movement performed on request, is known as *motor perseveration.*

Under abnormal conduct are included also the various impulsive acts due to temporary psychomotor over-valuation, in which the patients suddenly, and apparently imperatively, are led to perform simple and compound movements of various sorts. When these are caused by strong emotions (anxiety, anger, lust), they are known as *impulsive emotional acts* or instinctive acts.

In psychasthenic states, various *imperative acts* are encountered, usually as a result of abnormal fears; thus the fear of contamination with dirt or with bacteria leads to a continued washing of the hands and cleansing of the clothes. From the so-called *flight impulse,* "fugue" patients, usually from anxiety, suddenly undertake long trips away from home. *Dipsomania,* in which persons usually abstinent are suddenly seized with a pathological and irresistible desire for alcohol; the irresistible impulse to steal (*kleptomania*), or to incendiarism (*pyromania*), as well as *satyriasis* and *nymphomania* belong here.

Another disturbance of the will is to be seen in the abnormal tendency to be influenced excessively by other wills. A marked example is the condition known as the *hypnotic state.* Another instance is the so-called *command-automatism* of dementia praecox, where the patients will repeat movements, such as the clapping of the hands, made before them (*echopraxia, echokinesis*), or will repeat words heard (*echolalia*).

In the sexual domain, among the forms of pathological conduct met with, are a tendency to inflict pain (*sadism*) and to receive injury (*masochism*), as a sexual stimulus. In *exhibitionism,* the sexual feelings are increased by unseemly exposure of the sexual organs. The excitation of sexual feelings by inspection or palpation of various parts of the body or of pieces of clothing of the opposite sex is known as *fetichism.* Persons that cut off hair, or pieces of dress, or that mutilate corpses, and men of "Jack-the-Ripper" type are probably victims of sadistic and fetichistic impulses.

*Masturbation* and *sodomy* are other examples of pathological conduct in the sexual domain.

There is, obviously, every transition among human beings from those whom we call "responsible," through the domain of "partial responsibility," to those whom we regard as wholly "irresponsible." The bearings of this field upon ethics and upon criminology are obvious. (See also, Disturbances of the Conative Functions, under Psychiatric Methods.)

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[Note.—See also references in Part XII, Section II.]

# D. Examination of the Functions of the Efferent Paths that Influence Smooth Muscle, Heart Muscle, and Secreting Glands (Autonomic Neuron Systems)

## 1. Anatomical-physiological Notes

We know much more regarding the efferent than we do of the afferent neurons of the autonomic system. Thanks to the researches of Langley and others, it has been established that certain medullated centrifugal (preganglionic) fibers coming out of the central nervous system do not go directly to smooth muscle and glands, but end in arborizations around the cell-bodies of the neurons in ganglia outside

Fig. 550.—Red, Sympathetic Nerves; Blue, Craniosacral Autonomic, or Parasympathetic, Fibers, from the Oculomotorius. (After H. H. Meyer and R. Gottlieb, "Pharmacology, Clinical and Experimental," published by J. B. Lippincott Co., Philadelphia.)

the central system. The cells of the latter ganglia send their non-medullated axons (postganglionic fibers) to smooth muscle, heart muscle, or to secreting glands. What was formerly known as the sympathetic nervous system is now classified as a part of this great autonomic nervous system, so called on account of its relative independence of the central nervous system.

The efferent systems of the autonomic nervous system are conveniently grouped as follows:

### (*a*) *Mesencephalic Autonomic Neuron Systems*

Cells situated in the midbrain (mesencephalon), send preganglionic fibers, probably through the oculomotor nerve, to the ciliary ganglion. The cells in the latter

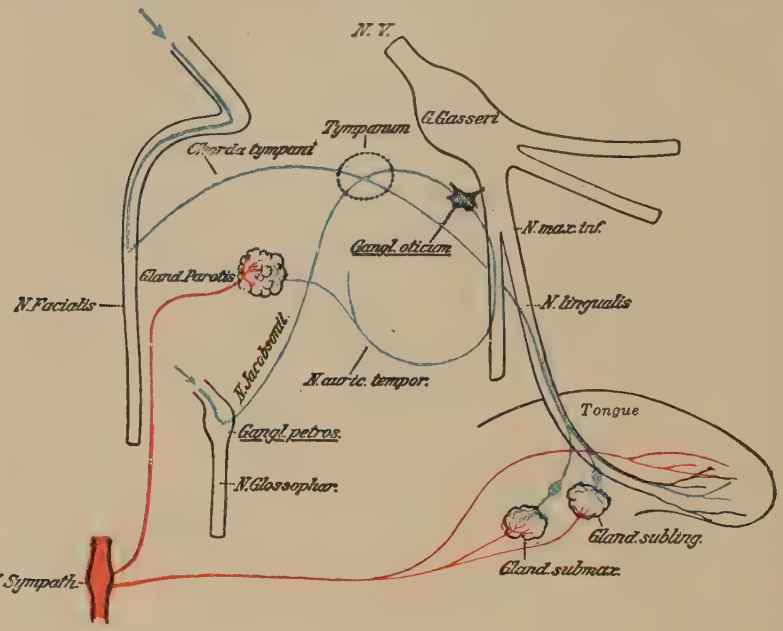


Fig. 551.—Innervation of Salivary Glands. Red, Sympathetic Nerves; Blue, Craniosacral Autonomic Nerves. (After H. H. Meyer and R. Gottlieb, "Pharmacology, Clinical and Experimental," published by J. B. Lippincott Co., Philadelphia.)

send axons (postganglionic fibers) to the M. ciliaris (which controls accommodation) and to the M. sphincter iridis (which contracts the pupil).

### (*b*) *Bulbar Autonomic Neuron Systems*

Here neurons, whose cell-bodies are situated in the medulla and pons, send their axons (preganglionic fibers) through the N. glossopharyngeus, N. vagus, and some possibly through the N. trigeminus and N. facialis, to peripheral autonomic ganglia in the head, neck, thorax and abdomen. Cell-bodies of neurons situated in these peripheral ganglia send their axons (postganglionic fibers) (1) to the heart muscle (inhibiting fibers of the vagus), (2) to the smooth muscle of the blood vessels (vasomotor nerves), the smooth muscles of the respiratory tract (tracheal and bronchial musculature) and, to some extent, the smooth muscle of the stomach and intestines, and (3) to various secreting glands (lacrimal, salivary, sudoriparous, respiratory, and digestive).

### (c) *The Spinal Autonomic Neuron Systems*

These may be divided into two groups:

(a) The cervico-thoraco-lumbar autonomic neuron systems, ordinarily spoken of as the sympathetic nervous system; and

(b) The sacral autonomic neuron systems.

The *cervico-thoraco-lumbar or sympathetic* group consists of neurons with cell-bodies in the spinal cord, probably the intermediolateral group of nerve cells in the gray matter, whose axons (preganglionic fibers) pass out through the anterior roots of the spinal nerves and thence, as rami communicantes, to the sympathetic ganglia, ending in them as arborizations upon cell-bodies situated there. From the cell-bodies of the latter neurons, the axons (postganglionic fibers) pass to the skin, to the viscera, and to glands, thus innervating heart-muscle, smooth muscle and secreting glandular tissue. The fibers going to the heart-muscle include the so-called accelerator nerves. The fibers going to the smooth muscle of the eye and eyelids, include the M. dilator iridis (which dilates the pupil), the M. orbitalis (which influences the prominence of the eye), and the smooth muscle of the lids themselves (which influences the width of the lid-slit). The fibers going to the smooth muscle of the blood vessels are the vasomotor nerves and especially the vasoconstrictors; it is possible that the vasodilators take a different course, since they emerge from the spinal cord through the posterior roots, not through the anterior. The fibers going to the smooth muscle of the hair-follicles or so-called pilomotor nerves, innervate the Mm. arrectores pilorum, contraction of which causes goose-skin. The fibers going to the smooth muscle of the stomach and intestines and of the walls of the large digestive gland ducts control the movements of the walls of these tubes. Other fibers go to the smooth muscle of the genito-urinary apparatus, including the ureters, bladder and urethra of both sexes, and in the male the scrotum and prostate, in the female the Fallopian tubes, uterus and vagina. The fibers going to the secreting glands, include those innervating the submaxillary gland, the sweat glands, and all the secreting glands of the digestive tract.

The *sacral autonomic neuron systems* include (a) vasomotor fibers, especially the vasodilators of the arteries of the rectum, anus and external genitals, including the important N. erigens, controlling the blood supply of the penis and clitoris; (b) the peristaltic fibers, controlling the contraction of the lower colon, the rectum and the bladder; and (c) certain secretory fibers, innervating the glands of the urethra, Bartholin's glands, etc.

The viscera are doubly innervated, on the one side by the sympathetic proper, and on the other by the craniosacral autonomic, or parasympathetic, system. Thus, the sympathetic innervation of the heart is through the accelerator nerves, the craniosacral innervation through the N. vagus. Similarly, the smooth muscle of the gastro-intestinal tract is doubly innervated; contraction is stimulated by the N. vagus, inhibited by the N. sympathicus. The pupil is also doubly supplied, the dilator fibers by the cervical sympathetic, the sphincter fibers by the midbrain autonomic.

Now such a double and reciprocally antagonistic innervation of the smooth muscle and secreting glands appears to hold throughout the whole body. The two antagonistic systems taken together were called, by Langley, the *autonomic nervous system.* The cervico-thoraco-lumbar part of this is the old sympathetic system; the rest of it is the craniosacral autonomic system, or, as some prefer to call it, the parasympathetic system. Physiologists and pharmacologists have thrown much light upon the opposing autonomic systems by experiments with electrical and chemical stimulation, the results of which are well shown in the following table:

| Effect of Sympathetic Stimulation | Effect of Atropin | Effect of Epinephrin | Organ | Effect of Pilocarpin | Effect of Ergotoxin | Effect of Craniosacral Autonomic Stimulation |
|---|---|---|---|---|---|---|
| | Paralyzes | ..... | Sphincter } Iridis. | Stimulates | ..... | Stimulates (N. III). |
| Stimulates (Th. I and II) | ..... | Stimulates | Dilator } | ..... | ..... | |
| | Paralyzes | ..... | M. ciliaris | Stimulates | ..... | Stimulates (N. III). |
| Stimulates (Th. I-III) | ..... | Stimulates | M. orbitalis (Mueller's) | Paralyzes | Paralyzes | |
| | Paralyzes | (Stimulates ‡) | Salivary glands | Stimulates | ..... | Stimulates chorda tympani. |
| Constricts (Th. II-IV) | ..... | Constricts | Cerebral blood vessels | ..... | ..... | Dilates (N. X). |
| | ..... | Dilates | Oral blood vessels | ..... | ..... | Constricts (N. IX). |
| Constricts (Th. II-IV) | Constricts (‡) | Constricts | Cutaneous blood vessels of head | ..... | ..... | |
| | Dilates | Dilates | Coronary blood vessels | Constricts | ..... | |
| Constricts (Th. II-L. IV) | ..... | Constricts | Intestinal blood vessels | ..... | Dilates | |
| Constricts (L. I-IV) | ..... | Constricts | Genital blood vessels | ..... | ..... | Dilates (N. pelvicus). |
| Stimulates (Th. II-L. IV) | Inhibits | Inhibits | Sweat glands | Stimulates | ..... | |
| Stimulates (Th. IV-VII) | ..... | Stimulates | Mm. arrectores pilorum (face) | ..... | Paralyzes | |
| Stimulates (Th. I-V) | Stimulates | Stimulates | Heart muscle | Inhibits | Inhibits | Inhibits (N. X). |
| Relaxes (Th. II-IV) | Relaxes | Relaxes | Esophagus | Excites | ..... | Excites (N. X) |
| Paralyzes (Th. II-L. IV) | Paralyzes | Paralyzes | Cardia | Excites | ..... | Excites (N. X). |
| Diminishes (Th. II-L. IV) | Diminishes | ..... | Tonus of stomach | Increases | ..... | Increases (N. X). |
| Paralyzes (Th. II-L. IV) | Paralyzes | Paralyzes | Peristalsis of stomach | Increases | ..... | Increases (N. X). |
| Diminishes (?) | Diminishes | Diminishes (?) | Secretion of stomach | Increases | ..... | Increases (N. X). |
| Inhibits (Th. II-L. IV) | Paralyzes | Paralyzes | Motility of intestine | Excites | ..... | Excites (N. X). |
| Relaxes (L. I-IV) | Relaxes | Relaxes | Colon | Excites | ..... | Excites (N. pelvicus). |
| Relaxes (L. I-IV) | Relaxes (?) | Relaxes | M. sphincter ani | Cramps | ..... | Cramps (N. pelvicus). |
| Relaxes (Th. II-L. IV) | Relaxes | Relaxes | Gall-bladder | Contracts | ..... | Contrasts (N. vagus). |
| Inhibits (?) | Inhibits | Inhibits | Pancreas secretion | Excites | ..... | Excites (N. X). |
| | Inhibits | Inhibits | Bronchial musculature | Excites | ..... | Excites (N. X). |
| Contracts (L. I-IV) | ..... | Contracts | M. sphincter vesicæ | ..... | ..... | Inhibits (N. pelvicus). |
| Relaxes (L. I-IV) | ..... | Relaxes | M. detrusor vesicæ | ..... | ..... | Contracts (N. pelvicus). |
| | ..... | Contracts | Uterus (pregnancy) | Relaxes | ..... | |
| | ..... | Relaxes | Uterus (gravid) | Contracts | ..... | |
| Contracts (L. I-IV) | ..... | Contracts | M. retractor penis | ..... | ..... | Relaxes (N. pelvicus). |
| Increases (Piqûre of Cl. Bernard) | ..... | Increases | Sugar tonus | Diminishes | ..... | |
| Increases (Piqûre vermis) | ..... | Increases | Heat tonus | ..... | ..... | |
| Contracts | ..... | Contracts | Pigment cells | Dilates | ..... | |

### (*d*) *Vagotonia and Sympathicotonia*

Under normal conditions, a sort of balance exists between the innervations in the two antagonistic systems, this balance being kept up probably by chemical action of hormones upon the nerve cells. Writing on the subject in 1913, I made the following comment:

"The balance maintained, normally, between the two antagonistic systems is one of the most interesting of physiological phenomena. Think, for example, of the rate of the heart beat—how constantly it is maintained at a given level in each person when the body is at rest; the impulses arriving through the vagal system just balance those arriving through the sympathetic system, so as to maintain a rate of approximately 72 beats per minute. And a similar balance is maintained in other autonomic domains (*e. g.,* pupils, bronchial musculature, gastric glands, gastro-intestinal muscle, sweat glands, bladder-muscle, etc.).

"This equilibrium is all the more remarkable when one considers how frequently it is temporarily upset in the exercise of physiological function. The play of the pupils with varying light, the watering of the mouth at the smell of savory food, the response of the heart to exercise and emotion, the flow of gastric juice on adequate stimulation, the opening of the bile duct at the call of the chyme, the transport of the colonic contents through one-third of the length of the colon through one vehement contraction every 8 hours, the sudden relaxation of the sphincter and contraction of the detrusor of the bladder in micturition, the violence of contractions in the domain of the N. pelvicus in parturition in the female and in ejaculation in the male, come to mind at once as examples of sudden physiological overthrow of balance."

Eppinger and Hess have introduced the clinical conceptions of vagotonia and of sympathicotonia. In *vagotonia* there is (1) a hypersensitiveness to pilocarpin, (2) a relative insusceptibility to sympathetic stimuli, and (3) various clinical symptoms indicating heightened tonus throughout the craniosacral autonomic system. In *sympathicotonia,* in turn, there is (1) a hypersensitiveness to epinephrin, (2) a relative insusceptibility to pilocarpin and atropin, and (3) various clinical signs of heightened tonus throughout the sympathetic system proper.

Clinically, an outspoken case of vagotonia may include a varying number of the following signs (corresponding to stimulations of the craniosacral system): small pupils, accommodation spasm, wide lid-slits, salivation, epiphora, profuse sweating, reddened face, cold and moist hands and feet, bradycardia, pulsus irregularis respiratorius, bronchial asthma, eosinophilia, hyperacidity, gastrospasm, cardiospasm, pylorospasm, spastic constipation, biliary colic of nervous origin, anal-sphincter cramp, pollakiuria, and priapism.

With Dr. Sladen, I have used the *pharmacodynamic method* as a test in the control of such cases. As a stimulant of the craniosacral (or "vagal") system we have given pilocarpin hypodermically in doses of 0.01 to 0.003 grams (gr. 1/6 to gr. 1/20), and as a paralysant of the same system, atropin hypodermically in doses of 0.001 to 0.00065 gram (gr. 1/50 to gr. 1/100). As a sympathetic stimulant we have used epinephrin (adrenalin) usually in doses of 1 mg. hypodermically. Some use for these tests 1 mg. atropin, 1 cg. pilocarpin and 1 c.c. of adrenalin solution (1:1000).

We found some patients who reacted in an outspoken way to both pilocarpin

and epinephrin, each of the two systems seeming to be hypersensitive. The *pilocarpin-sensitive* patients react with salivation, sweating, nausea, epiphora, flushing, and a fall in blood pressure. They react to atropin by palpitation, dryness of the mouth and throat, and precordial oppression. The *epinephrin-sensitive* patients, on being given epinephrin, react with tremor, sense of cold, rigor, glycosuria and rise in blood pressure.

An analysis of the various pharmacodynamic reactions observed in twenty-one cases in this way will be found in our published paper.

Our studies led us to agree with those that urge that the conception of vagotony be not too rigidly defined; we must be prepared to meet with exceptions as yet difficult to explain, and with deviations from the pharmacodynamical reactions that might be expected. Certain of the hormones may be less elective than the physiologists have taught us to believe; thus the occurrence of vagotonic signs mixed with sympathicotonic signs in the forms of Basedow's disease accompanied by outspoken psychic disturbances (von Noorden, Jr., and others), demand more careful study. As Higier wisely remarks, the new conceptions of vagotony and sympathicotony will doubtless undergo evolution like the majority of clinical conceptions in neurology. We can, nowadays, make a diagnosis of tabes, Basedow's disease, Parkinson's disease, or of multiple sclerosis, even in the absence of one or more of the original pathognomonic signs, or cardinal symptoms, described by their discoverers.

For therapy, as well as for diagnosis, clinical men will do well from now on to give due consideration to disturbances of the visceral nerves. In no part of internal medicine can more be expected from pharmacotherapy; we have at our disposal a host of agents—nicotin, atropin, pilocarpin, physostigmin, colchicin, adrenalin, cocain, ergotoxin, calcium, to mention only some of them—that have already been shown to act more or less electively; may we not hope that our clinics may find out how effectively to use them and others still to be discovered, in regulating the functions of the visceral nerves in at least many of the instances when these are disturbed.

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## 2. Autonomic Symptoms and Signs

It is convenient to have at hand the *symptoms and signs referable to different parts of the autonomic system,* as follows:

### (*a*) *Symptoms and Signs in the Head and Neck*

(a) *The Eyes.* These include (1) miosis and mydriasis; (2) accommodation-spasm and accommodation-paralysis; (3) widened and nar-

rowed lid-slits; (4) von Graefe's sign; (5) Dalrymple's sign; (6) infrequent winking (Stelwag); (7) insufficient maintenance of convergence (Mœbius); (8) exophthalmos and enophthalmos; (9) epiphora and dryness of the eyeballs; (10) Lœwi's test (positive adrenalin-mydriasis); (11) Argyll-Robertson pupil; (12) anisocoria.

(b) *In the Nose and Mouth.* (1) Excess of saliva with constant spitting; (2) dry mouth or xerostomia; (3) coryza vasomotoria.

(c) *In the Skin.* (*vide infra*).

(d) *In the Meninges.* Pain of vasomotor origin (cephalalgia; hemicrania).

### (*b*) *Symptoms and Signs Referable to the Respiratory System*

(1) Laryngismus and laryngeal crises; (2) asthmatic attacks; (3) pulsus irregularis respiratorius; (4) Aschner's phenomenon (pressure on the eyeballs stimulating first the trigeminus and then, reflexly, the vagus and leading to arrest of respiration in the expiratory phase, with slowing of the pulse), the oculocardiac reflex.

### (*c*) *Symptoms and Signs in the Circulatory System*

(1) Tachycardia; (2) bradycardia; (3) changes in conduction time (dromotropic disturbances); (4) pulsus irregularis extrasystolicus; (5) angina vasomotoria; (6) Aschner's phenomenon (*vide supra*); (7) changes in blood pressure; (8) peripheral hyperemias and anemias; (9) intermittent claudication; (10) dyspragia intermittens intestinalis; (11) acrocyanosis; (12) urticaria.

### (*d*) *Symptoms and Signs in the Digestive Apparatus*

(1) Esophagismus; (2) cardiospasm; (3) gastric neuroses (hyperacidity, achylia, gastrosuccorrhea, pylorospasm, gastrospasm, gastric atony); (4) atonic and spastic constipation, diarrhea nervosa, colica mucosa, anal sphincter spasm.

### (*e*) *Symptoms and Signs in the Urogenital System*

(1) Retention and incontinence of urine; (2) pollakiuria and tenesmus; (3) renal colic; (4) disturbances of libido, of erection, of ejaculation and of orgasm; (5) uterine atony and certain menstrual disturbances.

### (*f*) *Symptoms and Signs in the Cutaneous System*

(1) Goose-flesh; (2) trichopilar crises; (3) contractions of smooth muscle of tunica dartos and of nipple; (4) hyperhidrosis and anhidrosis (unilateral or bilateral); (5) bromidrosis; (6) vasoconstriction (pallor); (7) vasodilatation (erythema); (8) dermographismus.

### (g) *Symptoms and Signs Referable to the Hemopoietic, Metabolic, and Endocrine Organs*

(1) Eosinophilia; (2) eosinopenia; (3) lymphocytosis; (4) status thymicolymphaticus; (5) the pigmentations; (6) increased or diminished glucose-tolerance (glycosuria); (7) increased or diminished fat-tolerance (steatorrhea).

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## 3. Tests for Pupillary Reactions and for the Power of Accommodation

Most important, clinically, are the test of the light-reflex; the tests for the normally associated movement of contraction of the pupil on convergence, and on accommodation; the test for reflex dilatation of the pupil (ciliospinal reflex); test for the power of accommodation; tests for the function of the smooth muscle of the eyelids; tests for the associated movements of the eyeball and eyelid, and of the function of the M. orbitalis (Müller's muscle).

### (a) *Reflex Contraction of the Pupil to Light*

(*Optic-dynamic Reflex*)

The centripetal part of the reflex-arc is the retina and the N. opticus; the centrifugal part is the mesencephalic autonomic system (fibers running through the N. oculomotorius, ciliary ganglion, ciliary nerves to M. sphincter iridis). Fibers go from each eye to the centrifugal arc of

both eyes, since part of the pupillary fibers of the optic nerve cross in the chiasm, and part do not. Illumination of the retina, therefore, in one eye causes, not only contraction of the pupil of the same eye (homolateral reflex), but also contraction of the pupil of the other eye (heterolateral or consensual reflex).

Formerly, it was believed that the periphery of the retina as well as the region of the macula mediated the light reaction, and Wernicke on this hypothesis based his test for the hemiopic pupillary reaction in hemianopsia. The studies of C. Hess by very exact methods indicate, however, that the part of the retina possessing pupillomotor power measures only 4 mm. in the horizontal diameter, and only 2.5 mm. in the vertical diameter. Though these results have not yet met with full acceptance by control observers, it seems probable that the pupillomotor domain of the retina is central and small, and that but little, if any, reliance can be placed upon Wernicke's hemiopic reaction.

On testing (1) the **heterolateral** or **consensual reaction,** we ask the patient to stand in front of a window and to look at some distant object in diffuse daylight. We then place a hand over one of his eyes; normally, the pupil of his other eye will dilate, and if, after a few seconds, the hand be withdrawn, the pupil of the eye that has not been covered will again contract.

On testing (2) the **homolateral light-reaction,** sometimes called the direct reaction, we make the patient face a window, with both his eyes open, and tell him to look at a distant object; standing on one side of him, we close one of his eyes with one hand and then shade the eye that is to be tested with the other hand. After three or four seconds, this hand is quickly withdrawn. One then notes whether or not the pupil contracts, making sure that the patient has not, in the meantime, changed the focus of his eye, or converged.

If there be no reflex contraction on applying this test, or if the reaction be sluggish, it is well to test the reflex with artificial light in a dark room, by throwing light into the eye with the reflector of an ophthalmoscope, as nearly centrally as possible, rather than from the side, noting, at the same time, the behavior of the pupil. Very convenient, for this purpose, in private practice, is the small pocket electric light, which permits one to throw a strong light into the eye without going into a dark room.

### (*b*) *The Associated Movement of Contraction of the Pupil on Convergence, and on Accommodation*

(1) **Testing the Contraction of the Pupil on Convergence.**—When the eye converges, the two medial recti muscles contract together, and there is, normally, an associated movement of contraction of the pupil. This is not a reflex, but a true associated movement (synkinesia), the sphincter of the pupil taking part in the synergism. This contraction of the pupil on convergence is often retained when the light reflex is absent,

hence the great importance of making sure, on testing the light reflex, that the patient continuously looks at a distance, the eyes not converging.

(2) **Testing the Contraction of the Pupil on Accommodation for Near Vision.**—Ordinarily, accommodation is associated with convergence, but even when the medial recti are paralyzed, accommodation may not be paralyzed, and, in such cases, the pupils may contract on accommodation. When there is no convergence, we ask the patient to look, first, at a distance, and then, quickly, at the end of his nose, and we note whether or not the pupil contracts. When the pupil does not react to light, but does react on accommodation, it is an "Argyll-Robertson pupil" (*q. v.*).

### (c) *Reflex Dilatation of the Pupil*

(*Function of the M. dilator iridis, Ciliospinal Reflex*)

This may be tested in either one of two ways:

(1) On pinching or pricking the side of the neck, there follows, normally, dilatation of the pupil on the same side. The afferent limb of the arc is made up of the sensory fibers of the cervical (spinal) nerves; the efferent limb runs through the first (or second) thoracic spinal root into the cervical sympathetic.

(2) Drop into the eye to be tested a few minims of a 2 per cent solution of cocain hydrochlorate. This stimulates the endings of all the sympathetic nerves in the neighborhood, causing not only dilatation of the pupil, but also retraction of the upper lid, and slight exophthalmos. If the nerve endings of the sympathetic on the M. dilator are degenerated, no mydriasis follows the instillation of cocain.

### (d) *Disturbances of the Pupillary Reactions*

#### i. Changes in Shape and Size

An **irregular pupil** may be due to adhesions between the lens and the iris from iritis (synechiae), or to old injury, or to partial paralysis of the sphincter (in tabes and general paresis). An excentric position of the pupil may be due to adhesions, to an iridectomy, or it may be congenital (coloboma).

The **size of the pupil** varies much physiologically. The pupils are relatively small in the new-born, in old age, and in hypermetropia. They are relatively large in older children, and in myopia. When pupils are markedly small (*miosis*) or markedly large (*mydriasis*), a pathological condition should be suspected. One makes sure always, of course, that no miotic drug, such as eserin or pilocarpin, or mydriatic, such as atropin, cocain or euphthalmin, has been dropped into the eye before the examination, and that no drug influencing the size of the pupils has been

taken inwardly, since nicotin and morphin will contract the pupil, and belladonna, hyoscin and scopalamin, taken internally, will dilate it.

**Inequality of the pupils** (*anisocoria*) is an important sign, demanding most careful testing of the pupillary reactions. Inequality may depend, however, upon differences in the refractive media of the two eyes (anisometropia). A pathological anisocoria may depend upon a pathological miosis of one eye (paralysis of M. dilator iridis, due to a sympathetic lesion; loss of light-reaction in tabes and general paresis); or to a pathological mydriasis of one eye (stimulation of the dilator of the iris in sympathetic irritation; paralysis of the sphincter of the iris).

### ii. Loss of the Light Reflex

One must determine in what part of the reflex arc the interruption has occurred.

#### (1) *Unilateral Pupillary Rigidity*

**Lesion in the Centripetal Limb of the Reflex Arc.**—If illumination of the right eye cause no contraction of either the right or the left pupil, whereas illumination of the left eye causes contraction of both the left and the right pupil, the disturbance must lie in the centripetal path of the reflex arc; that is, in the retina or N. opticus of the right eye. Since vision will also be injured in this eye, this form of pupillary rigidity, which consists of the absence of the homolateral and heterolateral reflex from the one eye, with retention of both homolateral and heterolateral reflex when the other eye is illuminated, is known as *unilateral amaurotic rigidity.*

**Lesion in the Centrifugal Limb of the Reflex Arc.**—Now if the right pupil does not contract either on illumination of the right eye or of the left eye, but the left pupil contracts consensually from the right, then the disturbance must be in the centrifugal part of the reflex arc (midbrain autonomic fibers in N. oculomotorius, ciliary ganglion, or ciliary nerves). If so, the right pupil will be constantly wider than the left, and it will not contract on attempts at either convergence or accommodation (so-called *unilateral absolute rigidity* of the pupil). In some of these cases the lesion destroys the fibers going to both the M. sphincter iridis (pupil) and the M. ciliaris (accommodation); the condition is then known as *ophthalmoplegia interna.* In rare instances there may be a lesion of the centrifugal limb of the arc involving the contraction of the pupil but not injuring the fibers innervating the M. ciliaris at all; this condition is known as uncomplicated sphincter paralysis, or as *pure absolute pupillary rigidity.*

**Lesion Between the Centripetal Limb and the Centrifugal Limb of the Reflex Arc.**—If the right pupil does not react to light at all, either

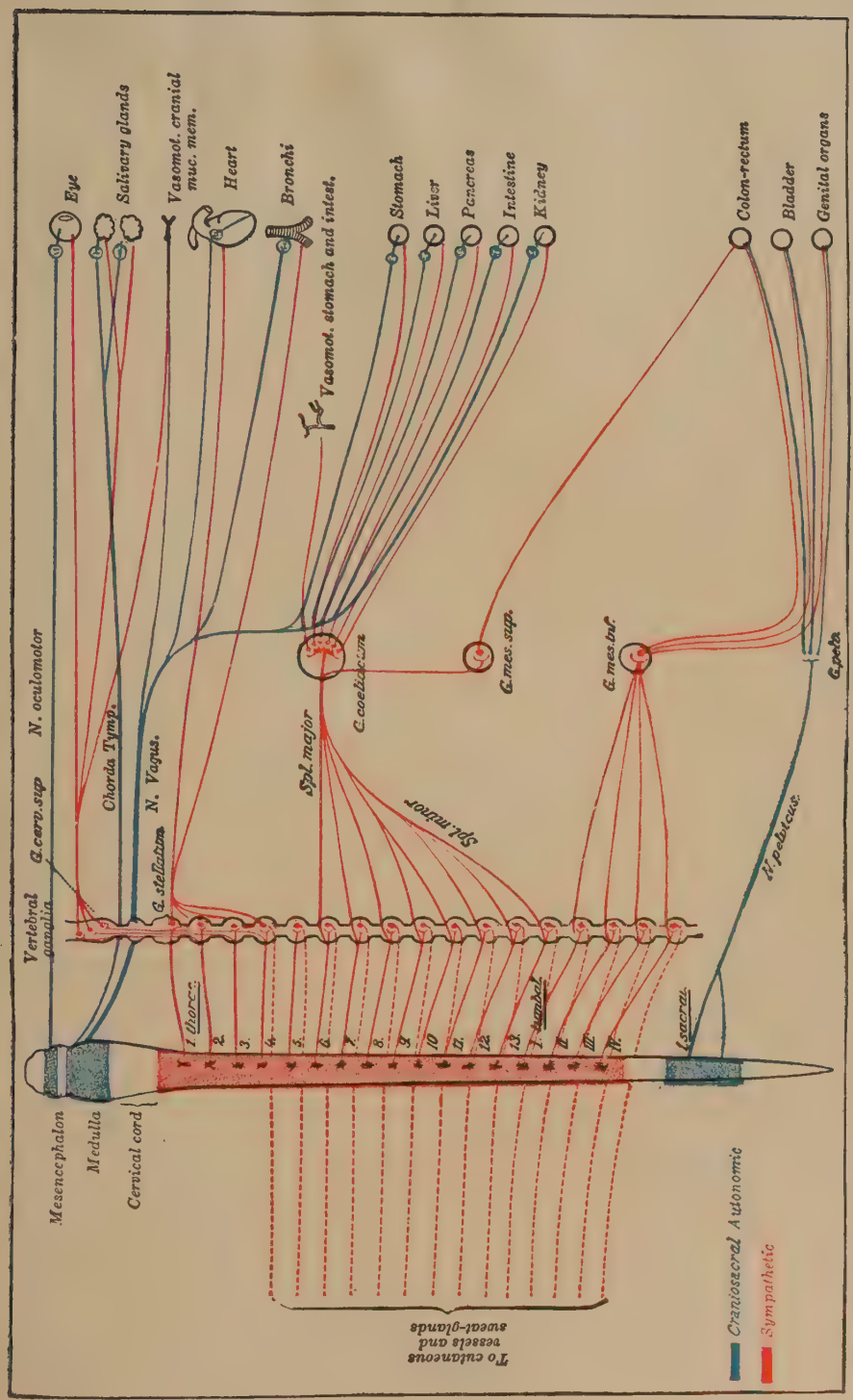


Fig. 552.—Diagram of the Autonomic or Vegetative Nervous System. The Sympathetic Innervation is in Red and the Craniosacral Autonomic in Blue. (After H. H. Meyer and R. Gottlieb, "Die Experimentelle Pharmakologie," published by Urban & Schwarzenberg, Berlin.

from illumination of the right or of the left eye, and yet will contract on accommodation and convergence, and the vision is good in both eyes, the disturbance must be either in fibers of the N. opticus after they have gone past the lateral geniculate body on their way to the midbrain, or in some associative path between the centripetal limb of the arc and its centrifugal limb, perhaps in neurons intercalated between the two (*Schaltneurone* of von Monakow), perhaps in the collaterals that go from the N. opticus to end in arborizations around the cell-bodies in the nucleus of origin of the centrifugal neurons (innervating the ciliary ganglion and, ultimately, the M. sphincter iridis). The condition is known as the *unilateral Argyll-Robertson pupil* or *unilateral reflex pupillary rigidity.*

### (2) *Bilateral Pupillary Rigidity*

When the light reaction, both homolateral and consensual, is lost in both eyes, we may be dealing with (1) *bilateral amaurotic rigidity*, if the patient be blind and the pupils still contract on convergence; with (2) *bilateral absolute rigidity*, if the patient's vision be good, but there be no contraction of the pupils on accommodation or on convergence; or with (3) *bilateral reflex rigidity* or *double Argyll-Robertson pupil,* if the vision be good and the pupils still contract on accommodation and on convergence.

It is to be kept in mind that combinations of these different kinds of pupillary rigidity may occur. Thus, for example, if the pupil do not contract on homolateral stimulation in either eye, while the consensual reaction is present in one eye, then the eye that, on illumination, yields a consensual contraction in the other eye must be the victim either of (1) absolute rigidity, in which case the pupil on that side will not contract on attempts at accommodation and convergence; or of (2) reflex rigidity, the accommodation-reaction being present; in the other eye, the rigidity will be amaurotic in type.

Injuries to the retina or to the optic nerve may cause amaurotic rigidity. It was long supposed that in lesion of one optic tract, there must be hemiopic rigidity (*Wernicke's hemiopic pupillary reaction*) when a ray of light is focussed upon the blind half of either retina; and that in hemianopsia, or hemi-opsia, due to pure lesions of the cortex, or of the occipitothalamic radiations, the pupillary reactions must be normal, since the pupillary paths through the optic nerves and tracts to the midbrain are not injured. Since the studies of Hess (*vide supra*) have shown that the pupillomotor area of the retina is central and very circumscribed, this test of Wernicke's has lost its anatomical foundation, a matter of satisfaction, doubtless, to the many clinicians that have tried to apply it in differential diagnosis, only to be disappointed in the result.

Reflex rigidity, or the *Argyll-Robertson pupil*, is most common in tabes dorsalis and in dementia paralytica. It nearly always means the onset of one of these two diseases, though it may precede other outspoken symptoms by years, or even by decades.

*Ophthalmoplegia interna* never occurs in "pure" tabes or dementia paralytica, but is very common in syphilis, rare in other organic diseases of the brain, and not uncommon from causes as yet wholly obscure.

*Pure absolute rigidity, i. e.,* uncomplicated sphincter paralysis, due either to nuclear or infranuclear lesion, is especially common in syphilis,

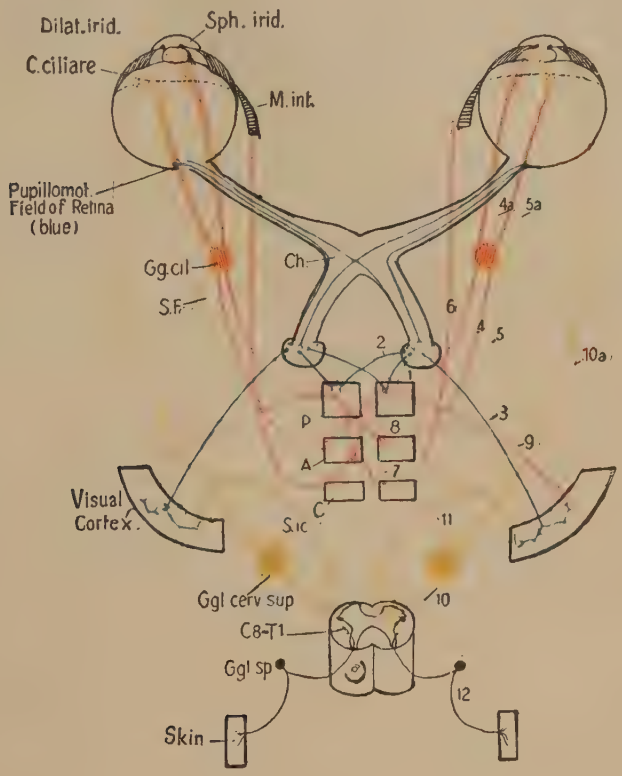


**Fig. 553.—Diagram of the Innervation of the Pupils.** Red = Fibers of N. III; Green = Sympathetic Ganglion and Fibers; Blue = Fibers of Optic Nerve Complex; M. int. = M. rectus int.; Sph. irid. = Sphincter iridis; Dilat. irid. = Dilator iridis; C. ciliare = Ciliary Body; Ch. = Chiasm; Gg. cil. = Ciliary Ganglion; S. F. = Sympathetic Fibers; S. i. c. = Intracentral Sympathetic Paths from Cortex to Ciliospinal Center in C8-T.; Ggl. cerv. sup. = Superior Cervical Ganglion; Ggl. sp. = Spinal Ganglion; P. = Pupillary Nucleus of N. III; A. = Accommodation Nucleus of N. III; C. = Convergence Nucleus of N. III. Paths for the Direct Light Reflex 1-4-4a—Homolateral; Consensual Light Reflex 2-4-4a—Contralateral. Reaction to Accommodation 8-4-4a—Bilateral. Convergence Reaction 7-4-4a—Bilateral. Perception Reflex for Light 9-4-4a—Bilateral. Pain Dilatation Reflex 12-10-10a. Emotional Dilatation Reflex, and Perception of Darkness 11-10-10a. (After O. Veraguth, "Die klin. Untersuch. Nervenkranker," published by J. F. Bergmann, Wiesbaden.)

occurs occasionally in tabes and in dementia paralytica, and, much more rarely, in senile dementia, alcoholism, and other organic diseases of the brain (Bumke).

### (*e*) *Power of Accommodation*

(*Vision for Near Objects, Function of the M. ciliaris*)

Having first corrected any error of refraction (important!), we test for the patient's "near point"; that is, the closest point to the eye at which minute objects, such as the finest print, can be distinguished. For normal young people, fine print should be distinguished at a distance of 10 or 15 cm. from the eye. If the power of accommodation be lost, we speak of *paralysis of accommodation* (lesions of N. oculomotorius, postdiphtheritic paralysis). If it be only weak, the condition is known as *accommodation-asthenopia*. One form of this is normal, namely, the gradually increasing inability to accommodate that begins to appear after the fortieth year (*presbyopia*), preventing reading at the ordinary distance (25 cm.) without spectacles; but this is due to loss of elasticity of the lens, rather than to paresis of the M. ciliaris.

The so-called *muscular asthenopia* is due to faulty convergence (medial recti), and not to weakness of the M. ciliaris.

### (*f*) *The Smooth Muscle of the Eyelids*

Sometimes the tonus of these muscles is continuously increased, as in the widened lid-slit of exophthalmic goiter. Overfunction of this smooth muscle can often be demonstrated by asking the patient suddenly to fix upon an object, for example, the finger held in front of the eyes; sudden widening of the lid-slit (*Dalrymple's sign*) may occur. The cocain test above referred to may also be applied.

### (*g*) *Tests for the Associated Movements of the Eyelid and the Eyeball*

Ordinarily, as the eye is raised or lowered, the upper lid follows it with equal pace. In conditions of hypertonicity of the smooth muscle of the upper lid, as in some cases of Basedow's disease, there may be a partial dissociation of these movements. One makes the test as follows: Asking the patient to fix his eyes upon the examiner's finger, the examiner moves this slowly up and down in front of the eyes. As the eyes go down, the eyelids do not follow the eyeballs with equal pace. As a result, the white of the sclera may show between the cornea and the upper lid (*von Graefe's sign*).

### (*h*) *The Function of the M. orbitalis* (*Müller's Muscle*) *Exophthalmos; Enophthalmos*

When Müller's muscle has its normal tonicity, the eye is normally prominent; if it be hypertonic, there is *exophthalmos*, or, better, *protrusio bulbi*; if it be hypotonic, there is *enophthalmos*, or retraction of the eye, with an incomplete

ptosis (pseudoptosis), due partly to the retraction of the eyeball, partly to the loss of tonicity of the smooth muscle of the upper lid, and usually associated with contracted pupil from loss of function of the dilator muscle of the iris (Horner's syndrome in paralysis of the cervical sympathetic).

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## 4. Disturbances of Innervation of the Heart and Blood Vessels

### (*a*) *Nervous Disturbances of Cardiomotility*

A slow pulse (bradycardia) may be due to excessive vagus stimulation. If so, the bradycardia will disappear a few minutes after the hypodermic administration of 1/80 or 1/60 grain of atropin. Bradycardia is a well-known sign in organic disease of the brain (vagus irritation). It is often due to reflex stimulation of the vagus from irritation of the intestinal tract (colica mucosa). A relative bradycardia is seen in typhoid fever.

A frequent pulse (*tachycardia*) may depend upon diminution of vagus stimulation, though it is probably more often the result of excessive stimulation by way of the accelerator nerves. Fever, neurasthenic states, and Graves's disease are conditions in which tachycardia is common; if they can be excluded as causes, one must think of myocardial disease and of cerebral disease as possible causes

### (b) *The Oculocardiac Reflex (Aschner's Phenomenon)*

On compressing the eyeballs, the pulse is normally slowed from 6 to 8 beats per minute. The centripetal impulses pass through the N. trigeminus, the centrifugal through the autonomic fibers of the N. vagus to the heart-ganglia.

In vagotonic states, the heart-rate may, on pressing upon the eyeballs, be slowed much more than in normal persons, often as much as 10 to 16 beats per minute. In sympathicotonic states, a paradoxical reflex may be met with, the pulse becoming accelerated rather than slowed on applying the test.

In the gastric neuroses, 1/5 of the cases show a slight slowing; 3/5 of the cases a slowing of 10 to 16 beats; 1/5 of the cases an acceleration of 20 to 30 beats (Loeper and Mougeot).

### (c) *Disturbances of Vasomotility*

Prolonged vasoconstriction of the skin causes pallor; vasodilation results in blushing. Theoretically, we have to consider the vasoconstrictor nerves and the vasodilator nerves, and, in turn, both paresis and spasm of the smooth muscle from under-action or over-action of each set of nerves. Clinical analysis cannot, as yet, be pushed thus far. It is to be hoped that before long the physiological studies of Porter of Boston may be found to be clinically applicable. In some patients the vasomotor nerves are particularly labile. In nervous young people, blushing and pallor are often excessive. Some patients suffer from vasomotor spasm (anginas, intermittent claudication, acroparesthesias, local syncopes of Raynaud's disease); others have vasomotor paralysis (acrocyanosis, erythromelalgia). It may be that increased permeability of the vessels is due to abnormal function of the vasomotor nerves (angioneurotic edema, hydrops articulorum intermittens, dermatographism, urticaria factitia).

Vasomotor anomalies are often associated with organic disease of the central nervous system. In cerebral hemiplegia, the paralyzed side, after initial hyperemia, is often cold, and the blood pressure may also be unilaterally lowered. A vasomotor form of jacksonian epilepsy has been described (Oppenheim).

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## 5. Disturbances of Innervation of Sweat Glands and Tear Glands

The function of the sweat glands may be disturbed locally, or generally.

One may try to make the patient sweat, either by asking him to sit in an electric-light cabinet for a few minutes, or by administering pilocarpin.

Some patients sweat too easily (*hyperidrosis*); others sweat but little (*hypoidrosis*). In local lesions, there may be areas in which there is no sweat secretion (*anidrosis*). Such an area of anidrosis, or of hyperidrosis, may be objectively recorded by the method of Purves Stewart; powdered charcoal is dusted on the skin; the charcoal sticks to the wet areas, and a photograph is taken.

The secretion of sweat is sometimes perverted. The sweat of some patients emits an extremely foul odor (*bromidrosis*).

The functions of the lacrimal gland may, like those of the sweat glands, be disturbed through nervous influences.

In vagotonics, excessive lacrimation with *epiphora* (overflow of tears to the face) may occur. In sympathicotonics, especially in some cases of Graves's disease, excessive dryness of the eyes is often complained of. I have recently seen a case in which very dry eyes accompanied a very dry mouth (*xerostomia*).

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## 6. Disturbances of Innervation of the Musculature and the Glands in the Respiratory System

The spasm of the smooth muscle of the bronchi is an important feature in bronchial asthma, and in acute and chronic bronchitis. In bronchitis this spasm is reflexly caused by irritation of the bronchioles. In bronchial asthma the spasm may be reflex from the nose, or the paranasal sinuses. In other cases, the spasm may be centrally irritated (toxic asthma).

The spasm of the bronchioles in anaphylaxis is sometimes due to stimulation of nerve cells in the brain. Some forms of asthma may be anaphylactic in origin.

The perversions of secretion of the glands in the respiratory system through autonomic influences have not yet been clinically analyzed.

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NOTE.—See also references under Bronchial Asthma. Pt. V.

## 7. Disturbances of Innervation of the Musculature and the Glands of the Digestive Apparatus

Here belong the disturbances of peristalsis (atony, hypermotility); also the spasmodic contractions of smooth muscle in the abdomen (cardiospasm, hour-glass stomach, pylorospasm, angina abdominis, colica mucosa, lead colic, hepatic colic, etc.). Disturbances of salivary, gastric, intestinal, hepatic, and pancreatic secretion due to autonomic innervations come also under this heading. These are described elsewhere.

The nervous mechanism of defecation is very much like that of micturition (*q. v.*).

In rectal paralysis there is retention of feces (*retentio alvi*); it is met with sometimes with brain tumors.

When the feces cannot be retained, we speak of incontinence of feces (*incontinentia alvi*). If the incontinence be intermittent, the lesion is probably above the center for defecation in the conus medullaris; if it be continuous ("dribbling"), it may be due to anesthesia of the rectum (*e. g.,* tabes) and loss of the internal anal reflex.

The reflex contraction of the non-striated internal sphincter may be tested by introducing the finger into the anus; under normal conditions, the finger will be tightly grasped by the M. sphincter internus. One has to distinguish between the *superficial anal reflex* involving the external sphincter (striped muscle) and the *deep or internal anal reflex* involving the internal sphincter (smooth muscle). If the finger be not firmly grasped, and, especially, if the anus remain open, "yawning" for a few seconds after the finger is withdrawn, the internal reflex is lost.

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NOTE.—See also references under Motility of Intestines. Pt. VIII.

## 8. Disturbances of Innervation of the Urogenital Apparatus

We shall consider briefly here the disturbances of autonomic innervation influencing (a) the secretion of the kidneys, (b) the motility of the pelvis of the kidney, the ureter and the urinary bladder, (c) the mechanisms of erection and ejaculation in the male, and (d) the mechanisms of ovulation, menstruation, and parturition in the female.

### (*a*) *Nervous Disturbances of Renal Secretion and Renal Vasomotility*

The study of these has only recently been begun. The kidney, like the other viscera, is doubly innervated by, apparently, reciprocally antagonistic systems—sympathetic and vagal. We shall probably soon know more about the polyurias and the oligurias of neural origin than we know now. We must learn to separate the influence of the vasomotor nerves in the renal blood vessels from the influence of the secretory nerves (proper) on the renal epithelium.

### (*b*) *Disturbances of Motility of the Renal Pelvis and Ureter*

The size of the renal pelvis and of the ureter can be studied *intra vitam* by means of collargol x-ray examinations (paralysis, spasm).

*Renal colic* and *ureteral colic* are due to spasm of the smooth muscle of the walls of the renal pelvis and of the ureter, respectively. This may be due to stone, to inflammatory irritation, or to kinking of the ureter (as in *Dietl's crises*).

### (*c*) *Disturbances of Motility of the Urinary Bladder*

The nervous mechanism of the filling and emptying of the urinary bladder is rather complex. There are three superimposed reflex-arcs: (1) peripheral autonomic in the plexus hypogastricus inferior of the sympathetic; (2) centripetal through the second, third and fourth sacral posterior roots to the centrum vesicospinale in the conus medullaris of the spinal cord ($S_3$-$S_4$) and thence (centrifugal) through the preganglionic fibers in the third and fourth sacral nerves into the N. pudendus and to the plexus hypogastricus interior, and thence through postganglionic fibers to the bladder; and (3) cerebralwards through the afferent paths to the somesthetic area of the cortex, and then, centrifugalwards, through the anterolateral funiculi of the cord to the centrum vesicospinale in the conus; these cerebral impulses simultaneously cause either (a) relaxation of the M. sphincter vesicae along with contraction of the M. detrusor, during *emptying* of the bladder, or (b) contraction of the M. sphincter and relaxation of the M. detrusor, during *filling*.

Normal retention of urine between acts of *micturition* seems to depend mainly upon the normal tonicity of the M. sphincter vesicae internus (smooth muscle). The external sphincter of the bladder, or M. constrictor urethrae (striped muscle) probably helps in the retention

by its normal tonicity, but has to do chiefly with the voluntary retention and with the interruption of the stream after it has been started. Micturition is voluntarily started, in the adult, by the prelum abdominis (contraction of the diaphragm and the abdominal walls) at the same time that the M. constrictor urethrae is relaxed. Once started, the M. detrusor continues to expel the urine, unless the stream be interrupted by voluntary contraction of the M. constrictor urethrae. When the cerebral arc is completely severed, owing to lesions in the brain or cord above the centrum vesicospinale in the conus, the voluntary control of the bladder

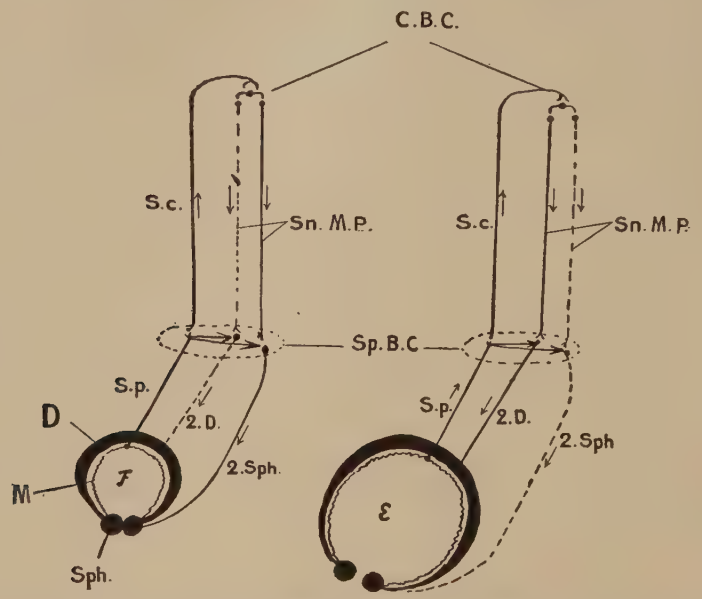


Fig. 554.—Diagram of Filling (*F*) and Emptying (*E*) of Bladder; Sph. = Sphincter vesicae; M = Mucous Membrane; D = Detrusor vesicae; S.p.-S.c. = Peripheral and Central Sensory Paths; Sn. M. P. = Supranuclear Motor Paths. 2. D. = to the Detrusor; 2. Sph. = to the Sphincter. Motor Path Marked - - - - - = Lowers Tonus. Motor Path Marked ——— = Raises Tone. Sp. B. C. = Spinal Center for Bladder. C. B. C. = Cerebral Center for Bladder. (After O. Veraguth, "Die klin. Untersuch. Nervenkranker," published by J. F. Bergmann, Wiesbaden.)

is lost as well as the sensation of fullness of the bladder. The vesicospinal arc and the subjacent autonomic arc then work automatically as in the new-born baby, with resulting *intermittent incontinence* or *reflex incontinence* of urine; as soon as the bladder becomes partially distended, the tension of the bladder wall excites reflex contraction of the detrusor and relaxation of the sphincter, and the urine is expelled in a jet. In rare cases of complete transverse lesion of the cord (above the conus), the reflex emptying of the bladder is abolished (like the other reflexes) and the bladder becomes distended (*retentio urinae*), sometimes causing rupture of the bladder, if the urine be not drawn off by catheter.

In rare cases an intermittent incontinence may be due to *cystospasm.*

In lesions of the conus medullaris involving the vesicospinal center, the disturbances are greater than in lesions above this area, owing especially to total paralysis of the M. constrictor urethrae (with loss of its tonus and degenerative atrophy). In some cases of total destruction of the conus, there is reflex incontinence (as in lesions higher up), mediated apparently by the peripheral (extraspinal) autonomic arc (L. R. Müller); this point is, however, in dispute, and the division of labor between the peripheral arc and the spinal arc is not yet fully understood.

In lesions of the peripheral autonomic arc (and, perhaps, of the spinal arc) true incontinence (*incontinentia vera*) results, owing to permanent relaxation of both the M. detrusor and the M. sphincter.

In anesthesia of the bladder wall, the bladder becomes insensitive to normal amounts of urine; the desire for micturition is not excited, and there is an initial retention (*ischuria*); as the bladder becomes overdistended, however, the urine, as a rule, mechanically dribbles away (*ischuria paradoxa*). This is seen often in tabetic patients, who always are found to have *residual urine* on catheterization; they expel the urine by contracting the abdominal walls, but the bladder is incompletely emptied. Sooner or later, overdistention, with constant dribbling, plagues the patient.

There may sometimes be retention of urine due to dulling of consciousness (coma, typhoid), to cramp of the sphincter, to an incapacity voluntarily to relax the sphincter, to stricture of the urethra, or to enlargement of the prostate.

Temporary retention of urine is common after operations, and in nervous patients under emotional stress (*psychogenic retention*); it is usually due to a cramp of the sphincter, and may often be relieved by a hot bath or hot compresses, or it may pass off after one or two catheterizations.

Some nervous patients with normal urine (absence of cystitis), are compelled to urinate very frequently (*pollakiuria nervosa*). Many children and young people are troubled with incontinence at night (*enuresis nocturna*); as a rule, a transitory and not a serious symptom, due to loss of cerebral inhibition in sleep, it is occasionally due to epilepsy.

In some psychoneurotic patients, more often in persons that have suffered some organic cerebral insult, the desire to urinate must be gratified at once, or involuntary micturition will occur (*imperative micturition*).

### (*d*) *Disturbances of the Motility and of the Vasomotility in the Genital Apparatus*

In the male there may be disturbances of (1) the scrotal reflex, (2) the mechanism of erection of the penis, and (3) the mechanism of ejaculation of the semen.

### i. The Scrotal Reflex

On stroking the perineum a few times with the handle of a percussion hammer, or on applying cold to it, or, gently, to the skin of the scrotum, the smooth muscle in the wall of the scrotum, the so-called tunica dartos, will in a few seconds contract; one sees a slow, wormlike contraction begin near the junction of the scrotum with the perineum, and extend slowly forwards. It is not to be confused with the cremaster reflex..

According to Curschmann it can be elicited as long as two hours after death!

### ii. Disturbances of the Mechanism of Erection of the Penis

Erection of the penis depends on (a) distention of the corpora cavernosa and spongiosa with blood (dilatation of arteries) and (b) increased consistence through prevention of the venous outflow by the tonic contraction of the M. transversus perinei, Mm. bulbocavernosi and ischiocavernosi. There are three physiological mechanisms that lead to erection; practically the three mechanisms are usually combined with one another: (1) *psychogenic,* path from cerebrum to upper lumbar cord and thence to pelvic sympathetic ganglia and peripheral organs; (2) *spinal reflex,* centripetal path from prepuce and glans through N. dorsalis penis and N. pudendus communis to sympathetic ganglia, and thence through posterior sacral roots into the cord, especially to the second and third sacral segments ($S_2$—$S_3$) (destruction of which abolishes this spinal reflex); thence, by centrifugal path, in roots of second and third sacral nerves through N. erigens to sympathetic ganglia and thence by postganglionic fibers to the smooth muscle of the walls of the arteries supplying the erectile tissue; at the same time, increased tonus in the muscles preventing the venous outflow ($S_3$); (3) *autonomic* (*extraspinal*) *reflex,* centripetal limb from walls of seminal vesicles (and urinary bladder) to ganglia in plexus hypogastricus; centrifugal limb from sympathetic ganglia to the arterial walls. Erection from this third mechanism occurs even after severance of the sympathetic ganglia from the spinal cord.

Lesion of the spinal cord below the upper lumbar region does not disturb psychogenic erection, but transverse lesions above the lumbar cord, say in the cervical or upper thoracic region tend to cause continuous erection (*priapism*).

Lesion of the spinal cord at the second sacral segment abolishes the spinal reflex erection, though "psychogenic" and "autonomic" erection may still occur.

### iii. Disturbances of the Mechanism of Ejaculation

This mechanism consists of two parts: (a) a first, or *autonomic, reflex,* in which the smooth muscle of the vasa deferentia, of the vesicae

seminalia, and of the prostata contracts and forces the semen into the urethra; and (b) a second *spinal reflex* leading to striped-muscle clonic spasm of the Mm. ischiocavernosi and Mm. bulbocavernosi, by which the semen is ejaculated from the prostatic portion of the urethra. This spinal reflex is mediated by the third sacral segment ($S_3$).

In diseases of the conus medullaris, along with loss of sensibility, it is the second part of ejaculation only that is interfered with (L. R. Müller), the semen being poured into the urethra still, through the autonomic reflex; owing to loss of the spinal reflex however, it is not thence ejaculated, but may flow out, drop by drop.

### iv. Impotentia coeundi

By this is meant an inability to perform the act of coitus.

This may be psychic in origin, when the reflex mechanisms are intact. Sometimes it is due to premature ejaculation (*ejaculatio praecox*), especially in neurasthenics, the semen being discharged before the physiologically necessary preliminary stimuli have acted in normal summation.

In total or *true impotence*, the power of erection is lost (tabes, conus lesions); in partial or *dissociated impotence*, there may be erection and orgasm without ejaculation; or ejaculation without orgasm (local lesions in conus, functional disorders).

### v. Pollutiones nimiae

The sexually abstinent adult has, normally, a reflex emptying of the seminal vesicles during sleep (nocturnal emission), about once a month. In sexual neurasthenics, such seminal emissions may occur more often, even in the daytime, with slight provocation.

Nocturnal emissions are known as *pollutiones nocturnae*, whereas emissions during the day independent of local stimuli are known as *pollutiones diurnae*, or *spermatorrhea*.

In the female, the secretion of Cowper's glands and of Bartholin's glands may be poured out either at night with erotic dreams, or, sometimes, in the day-time with erotic mental states; such discharges, not uncommon in psychoneurotic patients, are known as *pollutiones feminae*.

### vi. Genital Reflexes in the Female

These have, for obvious reasons, been less carefully studied than in the male. The innervation of the erectile tissue (clitoris) is doubtless similar to that of the erectile tissue in the male.

The autonomic innervation of the fallopian tube must be important in the transfer of the ovum from the ovary to the uterus.

The uterine contractions are largely automatic. Women with com-

plete destruction of the conus medullaris have given birth to children, the uterine contractions going on entirely through autonomic influences, independent of the spinal cord.

Impotentia coeundi in the female may sometimes be due to reflex spasm of the M. constrictor cunni (*vaginismus*).

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## 9. Disturbances of the Trophic Functions (Trophoneuroses)

The existence of distinct trophic nerves is still disputed.

The integrity of the lower motor neurons of the cerebrospinal system is certainly necessary for the nutrition of striped muscle. When they are injured the muscles innervated by them rapidly atrophy and show the electrical reaction of degeneration. Whether smooth muscle depends similarly upon the integrity of the efferent autonomic neuron systems we do not yet know. It would be interesting experimentally to injure the nerve fibers innervating the smooth muscle of the arteries and the intestines and watch the effect upon the muscle itself. I have sometimes thought it possible, from analogy, that striped muscle may also receive autonomic innervations, and that the trophic disturbances in degenerative atrophy in lesions of the motor nerves may be due to simultaneous injury to lesions of these autonomic innervations. This point should be investigated. It has been suggested that trophic influences are mediated by centrifugal conduction through the sensory neurons (Kohnstamm). Weir Mitchell believed that trophic disturbances in the skin and its adnexa are due to partial injuries of nerves.

Certain disturbances that have been attributed to trophic nerves have in reality been due apparently to loss of sensation from injury to ordinary sensory nerves, permitting parts to be injured without the knowledge of the patient, the normal reflex defensive mechanisms not being started up. Thus the injury to the eye following extirpation of the Gasserian ganglion does not follow if the eye be protected from injury. Many bed-sores could be prevented from developing by the avoidance of pressure. The opinion generally prevails, however, among physicians, that the nervous system in some way or another directly influences the nutrition of the tissues, and indirectly has a still greater influence through vasomotor and secretory effects (as in acromegaly, myxedema, Dercum's disease, etc.).

A most important contribution has been made by Head and Rivers, who severed cutaneous nerves in the skin and watched, first, the vasomotor and secretory disturbances, and, later (after two or three months), the trophic changes. A trophic ulcer healed only when the pain nerves regenerated. The studies of Head and Campbell on herpes zoster favor the view that there are not special trophic nerves, but that the trophic disturbances are due to irritation of the spinal ganglion cells. Studies on multiple neurotic gangrene of the skin have led Kreibich to the belief that the trophic changes are due to excitation of vasodilator centers.

According to Cassirer, trophic changes in the skin, bones and joints are due more to pathological alteration of innervation than to total loss of innervation. He thinks that the tissue cells ordinarily can get on without neural regulation, but that the latter becomes necessary when especial nutritional demands are made upon the cells.

Among the diseases still classified as trophoneuroses may be mentioned the bed-sores of myelitis (acute decubitus), progressive facial hemiatrophy or hemihypertrophy, poliomyelitis, tabetic and syringomyelic osteopathies and arthropathies, perforating ulcer of the foot in tabes, scleroderma, sclerodactylia, pigmentary disturbances of the skin, glossy skin, and painless whitlows (panaritium).

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# E. Examination of the Mental State; Elementary Psychiatric Methods

## 1. Introduction

Certain of the disturbances of the cerebral cortex are associated with abnormal mental manifestations; it is with these, especially, that psychiatry has to deal. The changes in the cortex are often so slight as to escape detection by microscopical methods of examination; indeed, they are in all probability in large part to be regarded as the results of biochemical and bio-physical processes in the cortical neurons. At present physical and chemical methods of examination are too undeveloped to permit of any satisfactory correlation of cortical lesions with the abnormal psychic processes that accompany them, and, for the present, we do best to study and to classify the abnormal mental manifestations for themselves.

It is necessary, therefore, to learn how (1) to test perception, and to recognize anomalies thereof; (2) to examine the intellectual processes, and to recognize intellectual defects; (3) to observe the expressions of the emotions, and to detect any abnormalities that may be present; and (4) to draw conclusions from the conduct or behavior of a patient as to his character and the conditions of what we call his "will."

Modern psychiatry has of late years undergone such marked development that a methodical testing of the psychic functions and a thorough analysis of the psychic changes manifested has become matter for the psychiatric specialist. (See text-books of psychiatry.) So many diseases of the bodily organs and of the nervous system are, however, associated with abnormal psychic manifestations, that the internist must be versed in at least the elementary methods of psychiatric examination and analysis. Moreover, the milder forms of mental disease, not at all, or scarcely, noticeable in ordinary social life, and of which the patient and his friends may be scarcely conscious, are met with first by the general practitioner or internist, or perhaps by the neurologist, long before there has been any thought of consulting a psychiatrist. Recognition at this stage is of

the greatest importance for prophylaxis, on the one hand, and, on the other, for special observation and treatment.

A general idea of the mental state of a patient may be gathered in the taking of the ordinary anamnesis. If psychic disturbances suggest themselves, opportunity should be taken to test the more important psychic functions more systematically, and, as far as possible, without hinting to the patient that anomalies of mentality are suspected.

In addition to the anamnesis, the speech, the writing and other movements of the patient, his general appearance and conduct, as well as certain vasomotor and secretory phenomena, may give clues as to the mental state. Keeping in mind the social stratum to which the patient belongs, and the individual differences that occur among persons in every social level, attention should be paid to certain points in external appearance (cleanliness or uncleanliness, neatness or negligence, simplicity or affectation, modesty or immodesty, aggressiveness or shyness, exaltation or depression, activity or relaxation, etc.). We note especially the spontaneous activities of the person, in contrast with the reactions exhibited on external stimulation (requests; mechanical, chemical, thermal and other stimuli).

Our examination will, perforce, be very different, according to the clearness, or fogginess, of the general consciousness of the patient. Thus, a patient in deep coma responds to no external stimuli; and, in cases of mental fog, the general consciousness may still be too obscured to permit of any extensive analysis of the mental state. Many persons, however, whose general consciousness appears perfectly clear, who comprehend our questions, give quick answers, and on superficial examination may seem very normal, may be found on analysis to be the victims of serious psychic anomalies (hallucinations, delusions, manias or suicidal impulses).

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[Note.—For references to larger texts on Psychiatry, see Part XII, Section III.]

## 2. Disturbances of Consciousness as a Whole

Clinically, we meet patients with every grade of awareness, from total unconsciousness, in which psychic phenomena are entirely in abeyance (though the purely vegetative, automatic and lower reflex nervous functions continue), through variable limitations of consciousness, to complete awareness.

### (a) *Sleep and Disorders of Sleep*

In normal persons, consciousness temporarily disappears, in whole or in part, during sleep; in deep sleep, we are probably wholly unconscious, but in light sleep consciousness, more or less clouded, continues in the form of dreams. The motor side is more affected in sleep than the sensory side, since sensory stimuli from the external world or from our bodies affect us, and become interwoven in our dreams, mingling with revived memories of recent or ancient events, in a wholly different way from that experienced while awake.

(1) **Analysis of Dreams.**—Modern neurology makes considerable use of dream-analysis in the effort to interpret nervous and psychic anomalies met with in patients; for neuropathic and psychopathic persons sometimes reveal, through their dreams, the effect of influences, feelings and ideas that they consciously or unconsciously suppress while awake, but that are of great importance for the understanding of their nervous and mental states (See English translation of Freud's "Interpretation of Dreams"). There seems to be an innate tendency in human beings to drive out of consciousness all painful, unpleasant or unconventional memories; and yet many of these (*e. g.,* painful experiences, quarrels, frights, domestic misunderstandings, erotic feelings) have a powerful

influence upon the mental life, exerting disturbing effects of which the patient himself may be entirely unconscious, or only dimly conscious.

(2) **Insomnia.**—The sleep of the patient should always be inquired into carefully. Sleeplessness, or insomnia, when not due to physical pain, to general bodily disturbance, or to emotional excitement, is usually dependent upon toxic, vascular or neural causes (circulatory insomnia, toxic insomnia, "nervous" insomnia). In insomnia of circulatory origin, we find either arterial hypertension (nephritis, atherosclerosis), or arterial hypotension (anemia, neurasthenia, tuberculosis). The insomnias of toxic origin are most often due to digestive disturbances, or to excesses in the use of alcohol, tea, coffee, or tobacco. The so-called nervous insomnias are usually due to nervous exhaustion from overwork or from an improper life. They are especially common in patients of neuropathic and psychopathic predisposition and in those suffering from hyperthyroidism.

(3) **Somnambulism.**—Children often, and adults occasionally, walk or talk in their sleep as a result of lively dreams. Somnambulism in children, especially if associated with night terrors (*pavor nocturnus*), should excite suspicion of the existence of adenoid vegetations in the nasopharynx, though they may be due to pathological irritability of the cerebral cortex. Somnambulism is most common in the hysterical.

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### (*b*) *Hypnotism*

A condition similar to that of normal sleep can be produced in suggestible persons; that is, in those whose psychic processes are abnormally easily influenced by an external will. The trances and twilight state of hysterical patients depend upon their suggestibility.

**Technic of Hypnosis.**—This requires self-confidence and experience on the part of the examiner. It is probably unwise to use hypnosis unless one takes the time and has the patience to attain to skill in the work.

The patient, especially if adult and intelligent, should be told to yield himself wholly to the hypnotic influence and to avoid all opposition to it, concentrating his mind on going to sleep and on any statements made to him by the physician. He should be seated comfortably in an easy chair, in a room in which the light is subdued, and told to fix his eyes upon some bright object held in front of him by the hypnotizer, who must compel the patient to believe that he is going to sleep. By concentrating the attention upon this, the suggestibility is heightened. Each hypnotist must work out his own methods, but it is customary to state, "You will soon be asleep now; your eyelids are growing heavy; it is hard for you to hold your eyes open." If the lids do not close of themselves, the hypnotizer may gently close them and then give the command, "Now go to sleep," informing the patient, however, that he will hear what the physician says to him.

According to the suggestibility of the patient and the skill of the hypnotizer, variable grades of the hypnotic state will be produced (somnambulistic state, lethargic state, cataleptic state), and it may be necessary to hypnotize the patient on successive occasions in order to attain to full hypnosis. I have found some patients very easy to hypnotize; others I have been wholly unable to influence. Hysterical patients are usually easily hypnotized. Typical psychasthenic patients in my experience are not easily accessible to hypnotic suggestion.

The patient once hypnotized, the physician may make such suggestions as he wishes to try; to hysterical patients he may say that the spasm or the paralysis, the pain or the anesthesia, of which he has complained, has vanished or will vanish at a certain time. It is generally better to treat one symptom at a *séance,* and in many cases one will be more successful by suggesting a gradual disappearance rather than a sudden disappearance of a symptom.

At the end of the *séance* the person can be awakened by a sharp command, "Now wake up," or simply by blowing upon his cheek, preceding the blowing by a statement to the patient that he will awake when he feels it.

If hypnotism be employed it should be used with the greatest care and conscientiousness. Some people seem to have been injured by it. Occasionally it is helpful in diagnosis. I remember especially one case presented by Dr. Hugh T. Patrick at the Chicago Neurological Society, in which the patient, who in his ordinary state had no memory of a fugue, after being hypnotized, told us all the details of his trip from Chicago into Indiana.

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### (c) *Coma*

The severest form of general disturbance of consciousness is called *coma*. The patient makes no voluntary movements. He lies with his limbs relaxed, making no response to his surroundings, his cheeks and alae nasi responding passively to the ingress and egress of air during respiration. The automatic respiratory and circulatory centers continue to function, though the breathing may be disturbed, sometimes being of the Cheyne-Stokes type. In deep coma, the superficial, deep and pupillary reflexes may be absent, the pupils themselves being either contracted or dilated; there is involuntary passage of the urine and feces, and the patient swallows neither food nor water. Painful stimuli may elicit no response, though, when the coma is less deep, certain pathological responses (*e. g.,* Babinski's phenomenon or the sucking-chewing reflex of Oppenheim) may come out. Coma occurs at the termination of many diseases in the so-called agonal stage; in intoxications (alcohol, anesthetics, morphin and other narcotics, septic diseases, intoxications from defective secretion like uremia and cholemia, or from disturbances of metabolism, as in diabetic coma); in prostration from heat, cold or starvation; in epilepsy; in apoplexy and other sudden cerebral insults; in encephalitis, meningitis, cerebral tumors, etc. A brief comatose state due to cerebral anemia from hemorrhage (hematemesis, menorrhagia, external wound), or from cerebral vasoconstriction in emotional states, or splanchnic vasodilatation in acute peritoneal injury, is known as a fainting-spell, or *syncope*. It is not to be forgotten that in epilepsy the patient's family nearly always speaks of his attacks as "fainting-spells" or "attacks of faintness." In true syncope, the unconsciousness is usually preceded by a brief period of vertigo and of optic disturbance, the patient saying that everything turned black before the eyes; during the syncope, the radial pulse may be absent, or only feebly palpable at the wrist. The syncopal attacks of the Stokes-Adams syndrome are due to the cerebral anemia dependent upon the extreme bradycardia of this disease.

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### (d) *Stupor*

In severe depressive states (manic-depressive insanity, some catatonic states, etc.), the patients may lie in a condition of stupor, making no spontaneous movements, the musculature presenting often a marked

hypertony (*catatonic rigidity, flexibilitas cerea*), or an abnormal relaxation and hypotony (*e. g., resolution*). They make no response to stimulation of the organs of special sense, though they may respond to questions or to cutaneous stimuli by raising the eyelids or by a slight movement of the head. They give the impression of being wholly ignorant of their surroundings (*disorientation*). Despite these symptoms, the cutaneous and deep reflexes and the pupillary reflexes may be retained and the sphincters kept under control. Such patients may swallow when fed, though some of them have to be fed through a stomach-tube.

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### (*e*) *Sopor*

When a patient, left undisturbed, sleeps very soundly, but can be partially awakened by very strong stimuli so that he will give brief answers to questions and perhaps perform some movements, though he quickly falls off to sleep again as soon as the stimulation is discontinued, the condition is known as *sopor*. Here the reflexes are retained, and certain spontaneous movements are performed; these are often of peculiar character, the patient picking at the bed-clothes (*carphologia*), making articulatory sounds (*muttering delirium*), scratching movements, movements toward the genitalia, or purposeless movements of the arms and legs. Sopor, so common in the acute infectious processes (*e. g.,* typhoid, pneumonia), often goes over, later, into coma.

### (*f*) *Somnolence, Twilight States*

(*Mental Fog*)

In certain diseases, mild grades of disturbance of consciousness as a whole are met with, leading to pathological sleepiness or somnolence, to mental cloudiness, sometimes called *mental fog,* or *twilight state.* The

patients may be unable to concentrate their attention and may be partly disoriented. Sometimes they react abnormally easily to external stimuli, becoming preternaturally suggestible. Such conditions are met with in the psychoneuroses (hysterical twilight states, epileptic twilight states), but are sometimes evidences of depression of the cerebral functions due to organic disease (*e. g.,* beginning increase of intracranial pressure in hydrocephalus, brain tumor, tuberculosis, meningitis, etc.).

In the *hysterical twilight states* and *hysterical trances*, expressive movements and attitudes may attain to an excess never observable when the patient's movements are subject to the inhibitory effects of higher cerebral control. Artists have utilized the expressions of emotions in the hysterical as models for the depiction of pure uninhibited emotional reactions. The "sleeping dancer" of Munich, whom I saw in 1904, could be made to exhibit many of these in hypnosis.

In *epileptic twilight states*, long journeys may be made or crimes committed. In contrast with the hysterical twilight states, the epileptic patient is wholly inaccessible, during the mental fog, to external mental influences.

### (*g*) *Deliria*

When consciousness as a whole is disturbed, there may be not only loss of knowledge of the surroundings (*disorientation*), due to depression of the psychic functions, but also symptoms of motor and sensory irritation, the patient having lively hallucinations due to irritation of the cortical sense-areas, and making abnormal movements (restlessness, screaming, violence), due to irritation of the motor cortex. Such a condition, known as *delirium,* is common in many febrile states (*e. g.,* typhoid fever, pneumonia, scarlet fever, meningitis). In chronic alcoholism, if the patient be suddenly deprived of alcohol, an abstinence-delirium develops (*delirium tremens*), characterized especially by peculiar optic hallucinations (visions of large numbers of small, black, moving objects). Special deliria are also met with in various psychoses (exhaustion psychosis after infections, puerperal psychosis).

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### (*h*) *Disorientation*

Normally, we can pay attention to our surroundings and recognize them, distinguishing our relations to other people, to time, and to place —we are oriented. This *normal orientation* depends (1) upon normal power of comprehension, (2) upon normal memory, and (3) upon normal judgment. The *apathetic disorientation* of dementia praecox, the *amnestic disorientation* of Korsakoff's disease and the *delusional disorientation* of many psychoses, are examples of disturbances of these various functions. Disorientation is associated with a peculiar and disagreeable feeling of perplexity.

**Tests for Orientation.**—We must test the patient's capacity to form normal ideas regarding (1) himself (*self-consciousness*), (2) his relations to the world around him (*spatial orientation*), and (3) regarding time (*temporal orientation*). A few simple questions will suffice. Thus we ask:

(1) What is your name?
(2) Where do you live?
(3) What is your occupation?
(4) What is your religion?
(5) What year is this? What month? What day of the month?
(6) What day of the week is this? What time of day?
(7) What place is this you are in?
(8) When did you come here?
(9) Who came here with you?
(10) Who is this standing next to you?

If a patient does not answer a question, we must not immediately conclude that he does not know the answer. He may know it, and yet not say it, as in the psychomotor retardation of manic-depressive insanity, or in the negativism of dementia praecox. Or the patient may consciously and intentionally avoid the correct answer, as in catatonic paralogia.

When a patient is completely disoriented as to the relation of his own person to the surrounding world, to space and to time, and his ideas are incoherent, we say that he is in a state of *confusion.* Confusional states are common in epilepsy, and in advanced stages of dementia paralytica; in the latter, loss of memory and of the power of critical judgment are important factors in the origin of the disorientation (Sommer).

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## 3. Disturbances of Perception and Identification

In ordinary sense perception, the sensations resulting from stimulation of the sense organs are combined with certain memories of previous similar sensations into a perception. In disturbances of perception, therefore, the cause may lie in the sensory element, on the one hand, or in the associated memory element, on the other, or in the process of assimilation of the two. Among the disturbances of perception may be mentioned (1) the sense deceptions known as hallucinations, pseudo-hallucinations and illusions, and (2) the various failures in recognition or identification (sensory aphasias and agnosias) due to the inability of sensory stimuli to revive the memories necessary for full perceptions and identification.

### (a) *Sense Deceptions*

#### i. Hallucinations

By hallucinations we mean perceptions that appear in consciousness without excitation of the sense organ concerned by an external object, due to internal irritation of the sensory or associative neuron systems. The patient has a lively sensory experience and is completely deceived as to the true origin of the sensory stimulation, referring it always to an objective cause outside himself; the visions he sees, the voices he hears, and the contacts he feels, are more real to him, though subjective in their origin, than are the sensory perception experiences of normal life.

Hallucinations may occur in any one of the various sense domains, including (1) visual hallucinations (*visions*), (2) auditory hallucinations (*akoasmata*, consisting of indefinite noises, and *phonemes* when voices are heard), (3) gustatory hallucinations, (4) olfactory hallucinations, (5) tactile or haptic hallucinations, (6) kinesthetic hallucinations (feelings of movement), and (7) visceral hallucinations.

#### ii. Pseudohallucinations

By pseudohallucinations are meant memories that are so lively as to possess almost the quality of perceptions, though the patients recognize that they are internal in origin, and do not attribute them to external stimuli.

#### iii. Illusions

Illusions arise when the perception resulting from actual stimulation of a sensory conduction path undergoes distortion; these are pathological when they are due to pathological processes in the cerebral cortex. Some of the visions in delirium tremens are illusions. External objects are wrongly interpreted. Harmless sounds may be interpreted as threats.

#### iv. Tests for the Presence of Sense Deceptions

We infer their presence, (1) from observation of the behavior of the patient, especially of his expressive movements (peculiar staring of the paranoiac hallucinant, the tense listening, or the stopping of the ears, of the patient who hears voices, the defensive, or aggressive, movements of the alcoholic or epileptic hallucinant); (2) from the response of the patient in speech, or writing, to questions asked. In the majority of cases, visual and auditory hallucinations are revealed in answer to the two questions: (1) Have you seen anything peculiar, for example, any strange visions? and (2) Have you heard voices speaking to you which you could not account for? Some secretive hallucinants will give false answers, but the majority will admit having seen the "visions" and heard the "voices."

### (b) *Sensory Aphasias and Agnosias*

When a patient is capable of sensory stimulation in a given domain, but, owing to the lack of sufficient revival of memories of previous similar experiences, or imperfect combination of the sensations with the memories, he is unable to recognize or identify the perception, he suffers from *mental anesthesia.*

These perceptions may have to deal with symbolic things (conventional, learned) like letters, words, figures, musical notes, gestures, in which case the mental anesthesia is known as a *sensory aphasia* (*e. g.,* alexia, word deafness); or the perceptions may deal with non-symbolic things, in which case the mental anesthesia is known as a *sensory asymbolia* (Meynert), or as an *agnosia* (Freund). Motor disturbances of similar sort occur, those of symbolic character being known as *motor aphasia* (Broca) and *agraphia,* those of non-symbolic character as *motor asymbolia* (Meynert) or *apraxia* (Steinthal, Gogol); these motor disturbances are described further on.

#### i. Loss of Power of Recognition or Identification in Visual Domains]

The agnostic disturbances in the visual domain may be either (1) sensory aphasic or (2) agnostic proper.

On the sensory aphasic side, the patient, while seeing letters, words, pictures, etc., does not understand their meaning and is unable, therefore, to read (*alexia*). This condition is not to be confused with the so-called *optic aphasia* (Freund), in which the patient cannot name objects that he sees, but, after feeling them, can give the name.

On the agnostic side proper (sensory asymbolia), we have to consider the so-called *mind-blindness* or *optic agnosia.* This is to be sharply distinguished from the so-called cortical blindness in which only visual perception is lost. In mind-blindness, the visual acuity is sufficient of itself to

permit of optic recognition and identification, but the patient fails to recognize objects seen because he has lost his visual memories, which give to his visual sensations a meaning and a value.

### ii. Loss of Power of Recognition or Identification in Acoustic Domains

Here the auditory acuity is great enough to permit of the recognition of the meaning of sounds, but the meaning is not recognized because of the loss of auditory memories or of the associations between auditory memories and those of other sense domains.

On the sensory aphasic side the patient may have *word-deafness*, having lost the power to understand (1) sounds of syllables, (2) the sense of words, or (3) the sense of sentences.

As *acoustic agnosia* proper, or *mind-deafness*, is designated the condition in which sounds other than those of speech are heard but are not understood. The condition has not yet been sufficiently studied, but seems undoubtedly to exist.

The so-called *amusia* occupies a position intermediate between the object-agnostic disturbances and the symbolic-agnostic disturbances; in such cases a patient may have lost the power to understand music, although he may still be able to sing.

### iii. Loss of Power of Recognition or Identification in Tactile Domains

Under the topic of stereognosis (*q. v.*) we have pointed out that, despite retained tactile sensation, there may be inability to recognize objects felt, owing to the loss of tactile memories. This condition is known as *tactile agnosia* (Wernicke's *Tastlähmung*). At least three forms may be distinguished (Liepmann), (1) loss of memory pictures of tactile sense proper, (2) inability to fuse the single impressions belonging to the total memory picture, (3) splitting off of the tactile memories from the memories of other sense domains, owing to lesions of associative paths. Thus, let us take an orange as an example. On palpation of the orange, we receive at first simple tactile impressions (perception), which call forth the tactile memories of an orange (primary identification), following upon which there arises a total memory picture of the object (including visual, gustatory and other sensations in addition to tactile), the so-called secondary identification. Any part of this process may be disturbed.

These tactile agnosias are due to lesions in the parietal lobe. The perceptive form seems to be due to lesion in the posterior central gyrus, while the associative form, or true tactile agnosia, follows lesions further back in the parietal lobe, perhaps just behind the posterior central gyrus.

The term *tactile aphasia* should be reserved for the very rare condition in which things felt cannot be named, though they are recognized in

nature and can be named when looked at; it is due, probably, to a lesion in the path connecting the tactile sense-area of the cortex with the speech-center. Some French observers have, unfortunately, used the term *aphasie tactile* in the sense of tactile agnosia.

Concerning olfactory, gustatory and vestibular agnosia we know as yet little or nothing.

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## 4. Disturbances of the Intellectual Functions

The old psychology subdivided the mental functions into (1) those of the intellect, (2) those of the emotions, and (3) those of the will. Modern psychology has shown the intimate interdependence of all three, yet, for convenience of description, an analysis based upon the three subdivisions is still useful. Under disturbances of the intellectual functions we shall consider those of (a) the attention, (b) the memory, and (c) ideation.

### (*a*) *Disorders of Attention*

Psychologists seem very much at sea in their efforts to explain the phenomena of attention. Everyone recognizes that of the many stimuli, conducted centripetalward from the organs of special sense, and from the bodily sense organs simultaneously to the brain, and capable of arousing sensations, certain only are attended to, at any given time, and utilized for the arousing of memories to combine with them in the formation of perceptions. We focus our attention, as we say, upon a particular group of sensations and memories, with resulting influence upon the current of association of ideas. The portions of the field of consciousness to which our attention is directed are said to be *focal,* while the rest of the field is *marginal,* in consciousness. The capacity for "paying attention," of directing thought toward a definite task (*vigility*) and of maintaining this

task despite intercurrent stimuli (*tenacity*) is of fundamental importance as a part of the capacity of acquiring memory pictures and ideas—the so-called *recording faculty*. Through it, our store of memories can be increased or supplemented. This faculty of recording is, however, independent of the faculty of revival of memories long since acquired.

The attention is faulty in all states in which the consciousness is clouded or befogged.

The associationists assume that the elementary psychic conditions that dominate the process of attention are subject to the laws that hold for the course of the association of ideas. Attention is, for them, not an especial activity, but simply a part of the association of ideas. Wundt, the father of "apperception-psychology," makes the association of ideas subordinate to attention and regards the latter as a special independent mental faculty, a sort of internal will-activity.

Attention may be pathologically increased or pathologically diminished, or inhibited as regards either vigility or tenacity. Lack of attention is usually shown in the progressive dementias. In idiocy and imbecility there is *aprosexia,* inability both to set and to maintain a task; hypovigility is combined with hypotenacity. The attention can be abnormally easily distracted, that is, changed in its direction (hypervigility), in chronic nervous exhaustion (acquired neurasthenia), in psychopathic states, and in outspoken maniacal states. The greater the distractibility, the more dirigible from without, the less thorough is the intellectual work. The term *hyperprosexia* or exaggerated attention, though often applied to the easily diverted feeble attention of the maniacal (increased tendency to change the task set, or hypervigility, with diminished tenacity), should be reserved for hypertenacity, the fixing of the attention in a given direction to the exclusion of other directions (*e. g.,* the proverbial absent-mindedness of the professor). In the depressive phase of manic-depressive insanity the attention may be thus pathologically chained to sad ideas; in hypochondriac states, to ideas of disease; in psychasthenic states, to the troublesome obsessions.

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### (*b*) *Disorders of Memory*

We distinguish between memories of recent events, dependent upon the recording faculty mentioned above, and memory in the narrower

sense, including all our earlier experiences, depending upon the firmness of fixation and ease of revival of past memories.

### i. Testing the Reproduction of Old Impressions

*(School Memories)*

This is best done by testing the school memories of the person (calculation; national, religious, geographical, and historical facts). We ask the patient the following questions:

1. Who discovered America? When?
2. Name the larger rivers of the United States.
3. Who was the first President of the United States?
4. Name the States in New England.
5. Repeat the multiplication table.
6. Subtract seven from one hundred, seven from the remainder, and so on.
7. Repeat the alphabet, the names of the days of the week, and of the month.
8. Repeat the Lord's Prayer and the Ten Commandments.

One can easily extend the series at will. For the sake of comparison, a uniform set of a few simple questions, such as the list recommended by Sommer is desirable. Memory tests are useful in differentiating the different forms of dementia. In the non-paralytic dementias, school mem-

Fig. 555.—Figures Used to Test Symbolic Intelligence, Since They Appeal to the Visual Understanding. (After O. Veraguth, "Die klin. Untersuch. Nervenkranker," published by J. F. Bergmann, Wiesbaden.)

ories are often very well retained, in marked contrast with dementia paralytica in which simple series of letters and numbers are often imperfectly remembered. In catatonic dementia, loss of school memories may be simulated by the grotesque irrelevancy (paralogia) exhibited in answering questions; in maniacal states it may be simulated by the discursiveness due to distractibility of attention and flight of ideas; in melancholia, the slowness of reply may deceive the examiner and make him think that memory is injured.

### ii. Testing the Reproduction of Recent Impressions

*(Recording Faculty)*

We ask the following questions:

1. Who came with you to this place?
2. What did you have for breakfast?
3. Where were you yesterday?
4. Where were you a week ago to-day?
5. Where were you last Christmas?

Recently, psychiatrists like Ranschburg and Boldt have provided us with special optic and acoustic tests of the recording faculty. They are briefly described in my article in the last volume of Osler and McCrae's "Modern Medicine."

The recording faculty, which has already been referred to under Attention, consists of two factors: (1) perception and (2) reproduction. It is most efficient in childhood, especially between the 12th and the 14th year.

When it becomes impaired, the faculty of recording numbers seems to go first. The recording faculty begins to go very early in dementia paralytica.

Loss of memory is known as *amnesia,* impairment as *hypomnesia,* exaggeration as *hypermnesia,* and perversion as *paramnesia.* Amnesia may be general or partial.

**General Amnesia.**—In general amnesia, we may have only an exaggeration of normal forgetfulness, inasmuch as our latent memory pictures depending upon protoplasmic conditions are subject to alteration, and finally to dissolution, as a result of the metabolic changes that go on in the cortical neurones. Frequent reproduction of ideas in some way renders the material traces, upon which memories depend, more firm. We can easily understand why destructive diseases of the cortex, like those occurring in dementia paralytica, in atherosclerosis, and in syphilis, should powerfully disturb the storing of memories. It is interesting, in such cases, that memories of the later experiences of life disappear, as a rule, before those of earlier experiences. The old man remembers the events of his childhood and youth, and talks about them, though he may have lost track entirely of the events of his later life.

**Partial Amnesias.**—These are isolated or elective defects, which involve certain groups only of the general store of memories (*e. g.,* loss of optic memory in optic agnosia, or auditory memory in auditory agnosia).

These agnosias have already been referred to (*vide supra*).

**Paramnesias.**—In the perversions of memory, several groups of disturbance are included: (1) memory misrepresentations, in which constituents of actual experience are pathologically rearranged in groups and asso-

ciatively united; (2) memory falsifications, in which the patient describes as experiences things that are wholly imaginary, having no counterpart in his past, though they appear to be reminiscences (*e. g., confabulation* in hysteria, in imbecility, in dementia paralytica and in senile dementia; *pseudoreminiscences* in Korsakoff's psychosis).

Closely related to these disturbances are (1) the *pathological lies,* met with in the degenerative psychoses, and (2) the so-called *pseudologia fantastica,* in which the fancy of the egoistic person is given free rein, and the most remarkable tales are concocted and related.

Another interesting disturbance of memory is that so often met with in psychasthenics, who suddenly feel in a given situation that they have experienced it some time before (*sentiment du déjà vu*). It is a disturbance of identification, sometimes lasting only a few moments, sometimes continuing for weeks or months, in which case the patient feels that he leads a sort of double life.

### iii. The Binet-Simon Tests, and Other Tests of Intelligence

For practical purposes, a rough-and-ready method for quickly testing the intelligence, especially of children, has been found to be of great importance. Too much should not be expected of such tests; their results at best are only very rough approximations, but with the modifications that have gradually grown up as regards their use, the Binet-Simon tests are very helpful.

In making such tests we must distinguish sharply between *memory* and *judgment.* We often meet with a good memory that has made the accumulation of many facts possible, though these facts may not be properly valued; in other instances, we meet with a natural endowment capable of valuing facts properly even in the absence of a large store-house of facts in the memory. In the feeble-minded we see, usually, both defects of memory and defects of judgment, though the memory is often less defective than the judgment. For this reason, methods of testing the intelligence that depend merely upon testing school-memories are insufficient.

Binet and Simon have devised a series of tests that give a fairly good idea of the intellectual capacities of children between the ages of three and thirteen years, obtainable in a very short time. These tests are not directed so much toward the knowledge ordinarily acquired at school, as toward knowledge obtained in everyday life. They include tests of the powers of observation, of the recording faculty, of the judgment, and of the power of combination.

#### (1) *The Binet-Simon Tests*

**Three Years Old.**

1. Where is your nose? Your eye? Your mouth?
2. Repeat sentences of six syllables. (*It rains. I am hungry.*)
3. Repeat two numerals ("6—4").
4. Show three Binet pictures representing some *people* and a *situation.* ("*What do you see?*") A child of three names the things, but does not describe actions.

**Four Years Old.**

1. Sex of child. (*"Are you a little boy or a little girl?"*)
2. Name familiar objects. A key, a knife, and a penny. (*"What is that thing?"*)
3. Repeat three numerals ("7—2—9").
4. Compare the length of two parallel lines, 3 cm. apart; one 5 cm., the other 6 cm. long. (*"Which is the longer line?"*)

**Five Years Old.**

1. Compare the weights of two blocks; 3 and 12 grams; 6 and 15 grams. (*"Which is the heavier?"*)
2. Copy a square of 3 or 4 cm.; with ink, not pencil.
3. Repeat sentences containing ten syllables. (*"His name is John. He is a very good boy."*)
4. Count, with the finger, four pennies placed in a row.
5. Game of "Patience" with two pieces. Cut a visiting card diagonally. Place a whole card on the table. Nearer the child place the two pieces with the two hypotenuses away from each other. (*"Put these two pieces together so that they will be like that uncut card."*)

**Six Years Old.**

1. Distinguish between morning and afternoon. (*"Is this morning or is it afternoon?"*)
2. Define known objects. (*"What is a fork? A table? A chair? A horse? A mama?"*)
3. Carry out three simple orders given simultaneously. (*"Do you see this key? Put it on that chair. Then shut the door. After that, bring me the box that is on the chair. Remember, first the key on the chair, then close the door, then bring the box."*)
4. Distinguish right and left. (*"Show me your right hand."* Later, *"Show me your left ear."*)
5. Make an esthetic comparison of 6 heads of women (Binet), in pairs. *"Which is the prettier?"*

**Seven Years Old.**

1. Count, with the finger, 13 pennies placed in a row.
2. Describe the same picture as used in age 3. The child should now be able to *describe* things instead of simply enumerating.
3. Finish an incomplete picture. Four unfinished sketches are shown the child. (*"What is lacking in that picture?"*)
4. Copy, with a pen, a drawing of a diamond-shaped figure.
5. Name four colors, touching successively a red, a blue, a green, and a yellow paper, 1 by 5 inches in size. (*"What is that color?"*) Normally completed in six seconds.

**Eight Years Old.**

1. Compare two things from memory. (*"What is the difference between a butterfly and a fly?" "Wood and glass?" "Paper and cloth?"*) Two of the three pairs should be answered correctly.
2. Count backwards from 20 to 1.
3. Name the days of the week in order.

4. Count one-cent and two-cent postage stamps placed in order as follows: 1, 1, 1, 2, 2, 2. (*"How much are they worth, or, How much money to buy them? Count."*)
5. Repeat 5 numerals ("4—7—3—9—5").

**Nine Years Old.**

1. Make change—9 cents out of 25.
2. Define common objects other than by "use".
3. Name the day of the week, the month, the day of the month, and the year.
4. Recite the months of the year in order within 15 seconds.
5. Arrange 5 weights in order. Use 5 wooden cubes of same size and appearance, but loaded so as to weigh 6, 9, 12, 15 and 18 grams. Time limit, three minutes.

**Ten Years Old.**

1. Name 9 pieces of money—cent, nickel, dime, quarter, half-dollar, one dollar, two dollars, five dollars, ten dollars (in regular order). Have the child point with the finger and name each piece as he points.
2. Draw a simple design from memory.
3. Repeat 6 numerals (*e. g.*, 8—5—4—7—2—6). Make three tests.
4. Answer simple questions involving everyday problems.
5. Use three given words in a sentence (*e. g., Baltimore, money, river*).

**Eleven Years Old.**

1. Criticize sentences containing some absurd or ridiculous expression.
2. Use three words in a sentence.
3. Say 60 words in three minutes. (*"Say as many words as you can in three minutes; like table, board, beard, shirt, carriage."*
4. Make rhymes for given words.
5. Put words in order. (*"Make a sentence out of these words."*)

**Twelve Years Old.**

1. Repeat 7 numerals (2—9—4—6—3—7—5; 1—6—9—5—8—4—7; 9—2—8—5—1—6—4.
2. Define abstract terms. (*"What is charity? Justice? Goodness?"*)
3. Repeat a sentence of 26 syllables. (*"The other day I saw in the street a pretty young dog. Little Maurice has got spots on his new apron."*)
4. Resist suggestion.
5. Problem of various facts. (*"What is it?"*)

**Fifteen Years Old and Adults.**

1. Cutting-out test. Have the child watch the folding of a sheet of paper in four. With scissors cut a small triangle from one edge—the edge that does not open. Ask him to draw a picture of the paper as it will look when unfolded.
2. The reversed triangle. Cut a visiting-card along the diagonal. Ask the child to describe the resulting shape if one of the triangles were turned about and placed so that its short leg was on the other hypotenuse and its right angle at the smaller of the two acute angles.

3. Differences. Ask the difference between:

*Pleasure and honor.*
*Evolution and revolution.*
*Poverty and misery.*
*Pride and pretention.*

4. Difference between President and King.
5. Give sense of a selection read aloud.

For the full details of these tests see Town's translation, and especially for the desirable modifications introduced by Goddard, see the Binet-Simon Measuring Scale for Intelligence. Revised edition, 1911.*

### (2) *The Yerkes-Bridges Point-scale*

This scale, particularly suited to work with pre-adolescents, is a point-scale and not an age-scale, the tests being arranged in order of difficulty. It originated in the Huey scale. No matter what the age of the person under examination, be it the third year of childhood, a 12-year-old boy at puberty, or a 30-year-old adult, the examiner begins with the first test and proceeds through the entire series, or at least far enough to satisfy himself that the limit of mental attainment of the person under examination has been reached. Properly carried out, the principal intellectual functions are subjected to test.

After the point-scale examination has been made, the results may be expressed (1) by the "score," (2) by the "mental age" as determined, and (3) by the so-called "coefficient of mental ability," all three expressions appearing on the record-sheet.

To take an example given by Miss Hardwick, let us assume that a subject twelve years old scores 68 points. The examiner writes "68" after the phrase "total credits" at the top of the record blank. The graph shows 68 to be the norm for 11.3 years, and "11.3" is therefore registered as the "mental age." The norm for the subject's chronological age is seen in the graph to be 77 points; his coefficient of mental ability is then 68/77 or 88 per cent. The coefficient is entered on the same line with the score, the norm being written on the line below.

In working with the Yerkes-Bridges point-scale, the examiner should be familiar with Healy and Fernald's monograph, and also with that of Yerkes, Bridges and Hardwick.

### (3) *Other Mental Tests*

In addition to the methods above mentioned, students in this field now make us of:

(1) The so-called *Healy tests* (*q. v.*), consisting of moves on form boards, completion of pictures, memories of observations, picture-puzzles, etc.

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[*On sale at the Training School, Vineland, N. J. Price 15 cents. Pictures and other materials useful for the Binet tests can be obtained of C. H. Stoelting, 121 N. Greene St., Chicago.]

(2) The *Knox scale,* developed at Ellis Island for the examination of illiterate aliens.

(3) Certain *miscellaneous tests* for attention, rhythm, memory, analysis, imagination, judgment and feeling.

A good epitome of these methods of testing, together with the bibliography, will be found in the article by Rose S. Hardwick (see References).

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### (c) *Disorders of Ideation, Intelligence, and Judgment*

Though workers in normal psychology have long been interested in the phenomena connected with the association of ideas, it is only relatively recently that neurologists and psychiatrists have begun adequately to value association-tests in their work.

#### i. Tests of Association

We use a list of about one hundred stimulus-words, consisting of nouns, adjectives and verbs, and including abstract and concrete words, words that will apply to the various relations of life, but we mix these words up with one another so that words of similar significance shall not follow one another. With stop-watch in hand, one gives the patient a test-word and asks him to give expression immediately to whatever comes into his head. From the *nature of the associations* the test-words call up, and from the *time of the reaction* for each word, important conclusions can be drawn regarding (1) the intellectual capacities of the patient, and (2) the feelings and emotions that influence his thought. Test-words that for any reason arouse an unpleasant feeling (or negative feeling-tone), as, for example, those associated with unpleasant past experiences (quarrels, fears, sexual matters) are often not replied to promptly, but only after a considerable delay, and, when the response does come, it is often unusual and unexpected in character (Jung). The existence of such unpleasant feeling-tones may often be recognized by the psychogalvanic test of Veraguth.

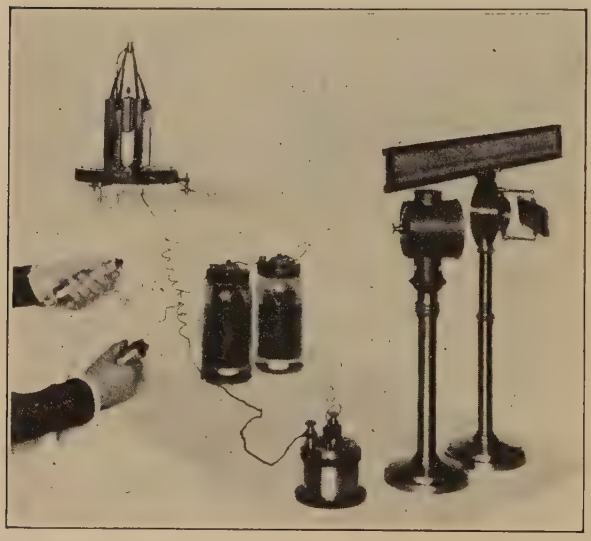

Fig. 556.—The Apparatus for Conducting a Psychogalvanic Examination. The Patient Holds in His Hands Two Metal Electrodes That Are Connected with Two Leclanché Cells and a Galvanometer. A Rheostat is Included in the Circuit. The Lamp and Scales Serve to Record the Fluctuations of the Galvanometer. (After O. Veraguth, "Die klin. Untersuch. Nervenkranker," published by J. F. Bergmann, Wiesbaden.)

The following list of words will be found convenient in making these tests:

| | | | | |
|---|---|---|---|---|
| 1 Head | 21 Ink | 41 Money | 61 Law | 81 Decency |
| 2 Green | 22 Bad | 42 Stupid | 62 Dear | 82 Narrow |
| 3 Water | 23 Needle | 43 Handle | 63 Glass | 83 Brother |
| 4 Prick | 24 Swim | 44 Suspect | 64 Quarrel | 84 Damage |
| 5 Angel | 25 Journey | 45 Finger | 65 Goat | 85 Stork |
| 6 Long | 26 Blue | 46 Dear | 66 Big | 86 False |
| 7 Ship | 27 Bread | 47 Bird | 67 Turnip | 87 Anxiety |
| 8 Count | 28 Sin | 48 Hold | 68 Paint | 88 Kiss |
| 9 Window | 29 Lamp | 49 Book | 69 Part | 89 Bride |
| 10 Friendly | 30 Rich | 50 Unjust | 70 Old | 90 Pure |
| 11 Table | 31 Tree | 51 Frog | 71 Flower | 91 Doors |
| 12 Question | 32 Sing | 52 Separate | 72 Strike | 92 Choose |
| 13 State | 33 Sympathy | 53 Hunger | 73 Box | 93 Hay |
| 14 Stubborn | 34 Yellow | 54 White | 74 Wild | 94 Content |
| 15 Stem | 35 Mountain | 55 Child | 75 Family | 95 Joke |
| 16 Dance | 36 Play | 56 Listen | 76 Wash | 96 Sleep |
| 17 Lake | 37 Salt | 57 Pencil | 77 Cow | 97 Month |
| 18 Sick | 38 New | 58 Sad | 78 Foreign | 98 Lovely |
| 19 Pride | 39 Custom | 59 Plum | 79 Fortune | 99 Dog |
| 20 Look | 40 Ride | 60 Marry | 80 Lie | 100 Scold |

The kinds of ideas that become associated with the given test-words may be classified as follows:

A. Sense of test-words correctly understood.

(a) Internal associations.

(1) Associations of spatial and temporal coëxistence.
(2) Predicative associations.
(3) Causality associations.

(b) External associations.

(1) Associations of spatial and temporal coëxistence.
(2) Identities.
(3) Speech-reminiscences.

B. Sense of test-words not understood.

(c) Test-words acting only through their sound.

(1) Word-supplements.
(2) Sound-associations and rhyme-associations. (A) Intelligible, (B) Nonsensical.

(d) Test-words acting only by setting free reactions.

(1) Repetition of test-word.
(2) Repetition of earlier reactions without sense.
(3) Associations for words used earlier.
(4) Reactions without recognizable connection.

Internal associations are those directed toward the sense of the test-word; external associations are those dependent upon custom, habit, speech, or sound-relations.

In predicative associations something is affirmed or asserted regarding the object; in casuality-associations there is a relation of cause and effect. In word-supplementation the reaction-word taken with the test-word makes up another word, a form of clang-reaction.

In mediate associations a connection between the test-word and the reaction can be understood by assuming some intermediate member of an association series (usually a clang-association).

Some observers classify reactions into those that are (1) objective, and (2) subjective or egocentric.

If more than sixty seconds elapse before an answer is given to the test-word, the result is designated as a "fault." Sometimes the only reaction is a repetition of the test-word. When an earlier test-word or reaction-word appears as a reaction, it is called perseveration. The number of repetitions and perseverations should be counted. When an association is spontaneously continued, either in an intelligent way or a nonsensical, we speak of discursive association.

For valuing the results of association tests we must refer to the monograph of Jung and to the papers of Aschaffenburg, Sommer, Jung and Riklin, and Isserlin.

### ii. Velocity of Association

In some instances, the association time may be abnormally shortened, in others, abnormally lengthened (*vide supra*). Even more important than the actual velocity of a given association is the rapidity with which a change in the direction of association occurs; thus, in the so-called *flight of ideas,* met with in mania, the patients talk with great rapidity, but the ideas given forth have only a superficial connection. Where the connection is better marked, though the impulse to talk is abnormally great, the condition is called *logorrhea.* An abnormal tendency to repetition of an idea once awakened in subsequent associations is known as *perseveration.* In some cases this perseveratory tendency is so marked that the same word or sentence may be repeated uninterruptedly for hours or even for days at a time (*e. g.,* in the nonsenical *verbigeration* of dementia praecox).

Some of the "brilliant" people of ordinary every-day life show slight hypomaniacal traits; everything is easy for them; they are restless, or very busy, people, with multiple superficial interests (*pressure of activity*).

Pathological slowing of associations is met with in the different forms of inhibition or so-called *psychomotor retardation.* This is most marked in conditions of so-called stupor. Here the associations are very slow. A sensation may be very slow in reviving a memory, and thus perception is made difficult; again, single ideas give rise only very slowly to other ideas normally in association with them, and it becomes difficult for the patient to pass through an associative series to a motor "goal-idea." This accounts for the slow, difficult speech in such cases, which, in extreme instances, may result in complete mutism. Similar difficulties are encountered in the use of the bodily musculature, and such patients may dress very slowly, sometimes requiring hours for the process. Sometimes the inhibition is so great that they lie for days and weeks in a state of complete relaxation (*resolution*), or in a state of hypertension and waxy flexibility (*catatonic rigidity*).

### iii. Pathological Dissociation of Ideas

(*Incoherence*)

In severe disturbances of association, the connections among ideas may be very seriously altered. There may be an entire absence of goal-ideas to direct the course of associations, as in the *incoherence* of dementia paralytica and of dementia senilis. Sudden and brief loosenings of the associations—so-called *sejunction* of Wernicke—may cause momentary lacunae in consciousness—the so-called *psychic deliquia* of L. Meyer; and these may form the starting-point of serious disturbances, leading to the formation of delusions. There is every gradation from such momentary dissociations to the more complete disorientations lasting for days, weeks or even months.

### iv. Intensity, Duration and Content of Ideas

Among the results of disturbances of the association of ideas may be mentioned the appearance of wholly abnormal ideas. We distinguish (1) exaggerated ideas, (2) imperative ideas, (3) autochthonous ideas and (4) the outspoken delusions.

(1) **The Exaggerated or Hyperdynamic Ideas.**—These include (a) single words or numbers that, without apparent reason, suddenly bob up in consciousness and disturb orderly thinking (*onomatomania*); (b) *hypochondriacal ideas* caused by abnormal visceral sensations; and (c) *premonitions.* The exaggerated ideas are not recognized by patients as intruders in consciousness, but are looked upon as an expression of their innermost nature; defending them, they feel themselves struggling for the maintenance of their personality.

(2) **Imperative Ideas or Obsessions.**—These include ideas that arising in the patient's consciousness are recognized by him as unjustifiable, nonsensical intruders. The patient says he knows the idea is absurd, but despite this, it recurs and troubles him. Examples are seen in the ideas associated with abnormal fears (*e. g.,* fear of places (*agoraphobia*), fear of contamination (*mysophobia*), fear of infection, fear of doing others an injury, etc.). They are frequently accompanied by negative feeling-tones. Patients subject to such imperative ideas are often the victims of *indecision,* and of the *doubting mania* (*folie du doute*). These phenomena are characteristic of the so-called psychasthenic states. In the severer forms, normal thinking is interrupted by the intrusion of all sorts of nonsensical questions, the so-called *mania of interrogation* (*e. g.,* Why are scissors called scissors?; Why has a chair four legs?; Why is gold a metal?). Patients are unable to rid themselves of the thoughts in spite of their desire to do so. Such a *mania of interrogation* would seem to be closely allied to the hebephrenic states (*q. v.*).

(3) **Autochthonous Ideas.**—In true *autochthonous ideas,* arising from pathological associative activity, the attention is, as in the imperative ideas, forcibly directed toward the ideas that are felt as troublesome intruders; but they differ from imperative ideas in that the latter are never regarded as foreign, as not belonging to the personality, and so do not have the dangerous significance for the whole mental life that attaches to autochthonous thoughts. The latter are closely related to hallucinations; indeed, the hearing of voices is sometimes preceded by a period in which autochthonous thoughts exist.

(4) **Delusions.**—The most important disturbance in the association of ideas is the falsification of content seen in delusions. In health, the intellectual activity, which leads to the formation of judgments and inferences through the association of ideas, depends upon the regular connection of the memory pictures with the perceptions corresponding to them coming from the external world and the body. Faulty judgments in health, known as mistakes, prejudices and superstitions, depend upon the admixture of personal experience with trains of thought current in a given community, or at a given time, and lying outside personal experience; in other words, our judgments are derived, partly from personal knowledge depending upon our perceptions and their memory pictures, but partly also from faith and beliefs, that is, from certain abstract chains of ideas supplemented by our fantasy.

Thus arise the various religious, scientific, social and political faiths. The feeling-tones accompanying such faith-ideas are unusually strong; the judgment is, consequently, much influenced by them. The greater the individual experience, and the better developed one's personal power in arranging knowledge in the formation of a judgment or an inference, the more independent the person will be in the judgments he forms; but the judgments of everyone, even the most intellectual person, are influenced by beliefs, since belief, or faith, is an absolute necessity for bridging over gulfs that could not be crossed if we were to try to form judgments based entirely upon personal experience. This explains why everyone is subject to mistakes, and why what we call knowledge is always undergoing alteration. There is every gradation from the mistake to which any normal brain is subject, to the "pathological mistake" met with in disease, which we call a delusion. No hard and fast line can be drawn between them; each is the result of a wrong train of thought that does not correspond to the facts of the external world.

Great care, therefore, should be taken in the examination of patients to make sure whether the environment of a patient can account for the origin of abnormal ideas in a brain that is not diseased, or whether the idea is one that could not arise in a normal brain exposed to the same environment. This task is not always easy. The beginner will be wise to describe as delusions, therefore, only ideas that are so grossly wrong as to be unmistakably the result of the activities of a pathological brain.

### v. Tests for the Presence of Pathological Ideas

Among the pathological ideas most important to recognize clinically we may mention: (1) *melancholic ideas,* associated with powerful negative feeling-tones (*e. g.,* suicidal ideas, ideas of poverty, ideas of self-depreciation, and other micromanic ideas); (2) *expansive ideas* (*e. g.,* delusions of grandeur, and other megalomanic ideas); (3) *ideas of reference,* in which the patient refers to himself words heard, or the behavior of others, when there is no justification for such reference; he may think that others are making fun of him, scoffing at him, scorning him, defaming him, etc.; (4) *ideas of persecution,* in which the patient thinks that others are treating him badly, that he does not get his deserts, or that conspiracies are formed against him.

Usually, such ideas can be unmasked by asking a few simple questions; namely, (1) Are you sad? (2) Has any one been making fun of you? (3) Have people treated you well? Has anybody "had it in" for you? (4) Are you sick? (5) Have you been unusually successful?

Patients usually cherish a delusion; it is hard, usually impossible, to convince them that the idea is false; they lack *disease-insight.*

In paranoid states, ideas of reference and ideas of persecution, associated with pathological egoism and an exaggerated consciousness of the self (personality) are characteristic. In the manic-depressive states, during the periods of exaltation, the patient is expansive, euphoric, megalomanic; during the periods of depression, he is sad, hypochondriacal, suicidal, sinful, poverty-stricken.

Delusions of grandeur are very common in the expansive state often met with in dementia paralytica.

It is not uncommon to have delusions arise as a result of the general weakness of judgment in idiocy and imbecility, and in the various dementing processes (*e. g.,* dementia praecox).

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## 5. Disturbances of the Affective Life

*(Feelings, Emotions and Moods)*

The intimate association of affective or emotional states with the intellectual activities has been seen above. It is desirable, however, in analyzing mental states, to pay some special attention to the feelings, emotions and moods. The tendency in the mind is to refer sensations, memories of sensations and ideas to external objects acting upon an observing subject, while the feelings, and the emotional states arising out of the feelings, are the more subjective elements of consciousness, and serve for building up that part of the content of consciousness that refers more particularly to the condition of the subject himself.

In neurological diagnosis, it will often be found that what causes pleasure and displeasure in life is the key to the understanding of puzzling nervous and mental states. The intellectual life of our patients is in high degree dependent upon feelings, moods and emotions; in other words, upon affective states, and upon the impulses to give expression to them. Only a few of the abnormal affective states can be mentioned here.

### (a) *Pathological Increase of Emotional Excitability*

This is seen, for example, in hysteria, in the irritability of neurasthenia, in the furor epilepticus, in the violence of alcoholic intoxication, in the anger of mania, and in the outbreaks of the senile or paralytic dement.

### (b) *Apathy*

Apathy, or depression of emotional excitability, is seen in the various forms of stupor, in the apathy of dementia praecox, and in that of imbecility. Sometimes the apathy shows itself in a lack only of the higher feelings (moral, esthetic).

### (c) *Exaltation or Hyperthymia*

In this state, positive feeling-tones (joy, excitement) accompany all the intellectual processes, even those that, under normal conditions, are only slightly pleasant, or even a little unpleasant. Among the best examples are the exaltation of mania, and of alcohol and drug intoxications, and the euphoria of dementia paralytica.

### (d) *Depression or Dysthymia*

Here the ordinary intellectual activities are accompanied by intense negative feeling-tones (discomfort and depression) leading to inhibition or to tension.

In normal life care, anxiety and bereavement cause sadness, but these stimuli, in pathological cases, give rise to excessive negative reactions, and even the stimuli that normally cause joyful reactions may not elicit them; hence in the depressive psychoses arise the micromanic delusions, the ideas of poverty, of unpardonable sin, of self-depreciation, and of the worthlessness of life. The patients assert that they have lost the interests that they formerly had, and they cannot understand why.

### (e) *Psycho-analysis*

Many imperious acts and imperative ideas are the result of the latent after-effect of exciting experiences, fears, and expectations. Important therapeutic results can sometimes be achieved in such states and in hysteria by "unearthing a hidden sorrow," or bringing into the focus of consciousness some long-forgotten painful experience, especially in sexual domains (psycho-analytic method of Freud; psycho-analysis of Jung).

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## 6. Disturbances of the Conative Functions (Will; Conduct)

Conduct and behavior have already been briefly referred to under Disturbances of the Higher Motor Functions. From the psychic side, however, some special mention of the functions of the will, observable in the conduct, behavior or style of the patient, seems desirable. We can judge of the mental processes of men in health and disease only through their motor reactions (including, of course, speech); that is, through the contractions of their muscles. Thus, the intensity and the quality

of the feelings reveal themselves in the expressive movements, those mimic, pantomimic or gesticulatory distortions of the face and limbs that are largely independent of what is ordinarily called the patient's will. The movements that result from a train of thought terminating in a so-called goal-idea are designated as *voluntary acts* or *deeds.* The whole conduct and demeanor of a person depends upon the chains of ideas terminating in such voluntary acts, and on the feelings and emotions, which, to a large extent, control the chains of ideas and also determine the expressive movements. A man's speech, his conduct, his behavior, his style in writing, speaking, dressing, etc., yield us the information that is obtainable regarding his conative functions.

What we ordinarily call a *strong will* or a *feeble will* depends upon the totality of affective and conative activities (character) of the person. But these affective-conative tendencies are in turn influenced by the intellect or cognitive faculty. Thus memory is necessary, in order that a voluntary act may be performed. The influence of partial losses of memory or voluntary activity is well seen in the aphasias and the apraxias.

### (*a*) *Suprapyramidal Disorders of Speech Movements, Writing Movements and Learned Movements of the Extremities*

Intermediate between the lower organic motor disturbances and the motor disturbances met with in the psychoses stand certain disorders of speech, of writing, and of non-symbolic movements of the extremities known as the aphasias, the agraphias, and the apraxias.

#### i. The Disorders of Speech Movements in the Aphasias

In the absence of anarthria or dysarthria (lesions of the pyramidal tracts or of the lower motor neurons), and of speech disturbances dependent upon the general mental state (coma, psychoses, hysteria), inability properly to perform the speech movements is known as aphasia.

The sensory aphasias, due to lack of understanding of speech, have already been referred to; in the disturbance of speech shown in the motor aphasias the difficulty is on the expressive rather than on the receptive side.

The severest forms of aphasia are those in which the power of speech is wholly abolished; the patients are actually dumb. Such complete abolition of speech-sound-making power is very rare; usually, even in the very severe cases, some words or phrases can still be spoken, and though the patients cannot talk, they may pronounce one or more words over and over again, residues of speech that Hughlings Jackson called "recurring utterances."

In the milder forms of aphasia, the power of speech may be only

slightly injured, and all gradations between these mild forms and the severest forms present themselves for study.

In studying the disturbances of the speech movements in the motor aphasias, we examine (1) the power of spontaneous speech, (2) the power of repeating what is heard, (3) the power of serial speech, and (4) the power of reading aloud.

### (1) *Disturbances of Spontaneous Speech*

Under spontaneous speech we include (a) ordinary spontaneous conversation (descriptions, expressions of desires, answers to questions), and (b) the naming of objects.

In *spontaneous conversation* the quantity of speech movements made should be noted. Some aphasics, with mild involvement, shun speech, even answering questions with great brevity; others seem to enjoy talking, the speech apparatus, once started, seeming not to find it easy to stop.

The qualitative changes are more important. As far as the content of the speech is concerned, two extremes are met with: in one, phrases with no words of concrete meaning, or only a few; in the other, almost exclusively words of concrete meaning are juxtaposed without small words or connectives (*akataphasia, agrammatismus*). The agrammatic cases have been further subdivided by French writers into (a) those with "telegraphic style," and (b) those with "negro style"; in the former, conjugation is retained, in the latter, not.

In nearly all cases conglomerates of syllables or letters occur, which at first seem to be utterly without significance; in the less marked instances of this, the clues can sometimes be discovered; in the severe forms, the whole expression is a jumble (*jargon-aphasia*).

In the *naming of objects,* it may be more difficult to find the word desired (from the sensory impressions) than in ordinary conversation (from association). Often when the right word cannot be found (*word-amnesia*), it will be recognized as right as soon as presented and can be correctly repeated. Substantives, especially concrete and proper names, give the most trouble; adjectives and verbs less.

Sometimes the patient, recognizing the object, but unable to name it, can help himself to find the word, by making movements illustrating the use of the object; but, even then, as a rule he confuses words (*verbal paraphasia*) or distorts them (*literal paraphasia*). In verbal paraphasia, a word used before, or one unsuccessfully sought before, may be spoken instead of the right word, a perseveratory phenomenon; or, a word associattively related (by sound, by coördination or subordination, by causality, by coexistence, etc.) may be produced. Literal paraphasia represents a severer disturbance than verbal paraphasia; syllables are displaced in the words, and letters in the syllables.

### (2) *Disturbances of Repetition*

Aside from true *echolalia,* or imperative repetition of words heard, a condition already referred to as occurring in the "tic" disease, we study in the aphasias (a) interrogatory repetition, and (b) repetition on direct request.

In *interrogatory repetition,* the patient, when asked a question, repeats it, often in a slightly different form; thus if asked, What is your name? he may say, What is my name? This form is evidently not far removed from echolalia.

In *repetition by direct request,* the patient repeats, at our request, the words we pronounce before him. He sometimes misunderstands our intent, and thinks that we are asking him a question.

In some cases, though spontaneous speech is greatly disturbed, everything heard can be correctly repeated, even difficult test-words; more often repetition is imperfect, short words being repeated usually better than long ones, though occasionally a patient who can repeat a long polysyllabic word perfectly will find it impossible to repeat a short sentence containing only monosyllabic words (Heilbronner).

Familiar words can be repeated better than unfamiliar words, or than words of a foreign language. Sometimes short words can be repeated better than the sounds of single letters (consonants). One should notice whether or not the patient tries to read the examiner's lips when under test, as this has an influence on the results obtained.

Entire loss of power of repetition does not occur except where the power of speech is practically abolished; attempts at repetition then result only in the expression of one of the residue-utterances, and, strange to say, if given such a residue-utterance as a task, the patient often fails to repeat it. The patients are often reluctant to try to repeat words; this is sometimes due to a misunderstanding of the examiner's intention, sometimes to a feeling of shame of their disability.

Sometimes a distortion of words (literal paraphasia) will appear on attempts at repetition, when no such distortion is noticeable in spontaneous conversation and only a little on naming objects. A confusion of words (verbal paraphasia) on attempts at repetition is not uncommon, often due to perseveration, sometimes to other associative cause. It is well to choose some words from a series (numbers, letters, days of week) as tests; not infrequently, instead of repeating the test word, the patient will react with another word from the same series (Monday, Thursday), or with a word from a different series (a letter, a number).

### (3) *Disturbances of Serial Speech*

Serial speech is very important in the study of aphasics; patients who can faultlessly reproduce series (letters, numbers, days of week, names of

months, prayers, poems) must be devoid of speech disturbance; moreover, in the milder aphasics, a study of the errors in serial speech will often yield clues to the nature of the disturbance, unobtainable by the tests of spontaneous speech and of the powers of repetition. Unfortunately, not every patient has had, normally, at his disposal, a large selection of series; moreover, it is not always easy to make the patient understand that we wish him to say the series to us. In trying to get him to count, if he does not understand our spoken request, we may make signs before him (rhythmical clapping, serial movements of the fingers, use of beads on a counting board, etc.); or to get him to say the days of the week, or the names of the months, we may make clear what we want by showing him a calendar.

We note whether on interruption in the course of a series, the patient can begin again where he left off, or must begin all over again; as a rule the series has to be given, as it were, automatically, *in toto*.

Omissions in a series are common; thus, either: . . . 23, 24, 25, 35, 36, 37 . . . or 37, 38, 39, 50, 51 . . . ; again, the patient may wander off into a different series, *e. g.*, 17, 18, 19, 20, 30, 40 . . . or Monday, Tuesday, February, March. Other examples are cited by Heilbronner.

### (4) *Disturbances of the Power of Reading Aloud*

Reading aloud is a complex process, involving both the receptive and the expressive side of speech; it is accordingly very often disturbed in aphasics. We have to think not only of the words and syllables as a whole (the phonetic word) but also of the words and syllables as made up of individual letters (orthographic or alphabetic word). It is well to find out first what the patient can do with letters as such, and then to see whether he can combine them with syllables and words and can pronounce the combinations; later we test the power to read sentences, both matter which is intelligible, and matter unintelligible to the patient. An inability to read (*alexia*) may be receptive, or expressive, in nature, or both.

## ii. The Disorders of Writing (Agraphia)

These may be hard to test if there be paralysis of the right arm; if there be only weakness, the patient may get on well enough with chalk and a blackboard; we may also encourage writing with the left hand (which will be found to be not infrequently mirror-writing). We examine (1) the writing without copy, either (a) spontaneously or (b) on dictation, and (2) the writing when the patient has a sample before him (copying).

### (1) *Writing Without Copy*

Most patients who can write anything spontaneously can usually copy in some way (either freely, or slavishly); inability to copy, when writing

without copy is possible, is very rare, occurring only in the so-called isolated, or pure, alexia.

In the severer disturbances, letters cannot be made on paper at all, nor can signs resembling letters be made; attempts at writing result only in lines and scratches, a meaningless scrawl. Some patients seem to have a memory of the forms of certain of the letters, but are unable to write these forms, showing discontent with their fruitless attempts; others seem content with their nonsensical scribbling and may even, subsequently, try to read aloud what they have written. Often a few letters are fairly well written at first, only to be followed by unintelligible strokes, hooks, and loops, some of these bearing a resemblance to one or more of the letters previously written (perseveration).

In the milder disturbances, two groups of cases are distinguishable: in one, the patient can write single letters he intends, or is asked, to write, though in general he is agraphic; in the other group, the patient cannot make single letters correctly on dictation. In case of failure, one must be sure that the task is understood; this is usually indicated by evidences of dissatisfaction with the effort made, and, especially, if among a set of printed or black letters, he can pick out the right one.

On trying to write words, the troubles with the letters reappear, though the patient's own name and even his address, may sometimes be written without error, when otherwise there is almost complete agraphia.

Writing is the most complex of all the speech-performances. Agraphic disturbances are more severe and less reparable as a rule than the disturbances of vocal speech.

### (2) *Writing from Sample (Copying)*

One sets a copy and asks the patient to write as nearly like the sample as possible.

### iii. The Disorders of Learned Movements other than Speech and Writing (Apraxias)

Speech and writing are, as we have seen, conventional and learned modes of expressing the contents of our ideas—they are symbolic in character. The suprapyramidal disturbances in this domain have been described as aphasic; suprapyramidal disturbances of the learned movements other than those of speech and writing are designated as apraxic. The normal condition in this domain is known as *praxia* or *eupraxia;* pathological conditions here are known as *apraxia* or *dyspraxia.* Our newer knowledge of apraxia is due largely to the researches of Liepmann, Pick, Bonhoeffer and Heilbronner.

In apraxia we see three main types of disturbance: (1) diminished spontaneity or almost total abolition of movement, despite the absence of

paralysis in the apraxic extremity; (2) distortions of movement in the apraxic part; and (3) confusions of movement, an entirely different act being performed than that intended.

### (1) *Absence or Diminution of Spontaneity of Movement*

This is best seen in unilateral apraxia of the upper extremity. The non-apraxic extremity may perform all complex actions without hesitation, while the apraxic extremity is quiet, except on special request, or when the patient is repeatedly reminded to make the movement. It seems as though the patient has to exert his will in an extraordinary way to make any movement, the apraxic limb acting, not like a part of the body, but rather as a complex instrument attached to the body, which the patient is beginning to learn how to use. When an object is placed in the apraxic hand of such a patient, he is prone to hold it tightly, even when it hurts him, and does not spontaneously lay it aside, though if asked to do so he usually can. The personal initiative seems to be lost for the apraxic limb, though not all patients show this phenomenon. Sometimes if the limb be placed passively in a given position the patient will not change the position of his own initiative, a condition simulating the waxy flexibility of catatonic states.

### (2) *Distortions of the Movements in Apraxic Extremities*

These distortions can be best demonstrated, as a rule, by asking the patient to perform certain complex movements in imitation of natural movements but without the presence of the natural object to which the movement pertains; thus, we may ask him to make the movement of shaking hands, of counting out money, of beckoning, of opening and closing a door, of leading an orchestra. The apraxic patient will make the most bizarre attempts at the movement, moving his fingers this way and that, twisting his joints, stopping as though in doubt, and starting all over again, the movements being so grotesque that they have been described as "grimacing of the extremities"; if the patient be not aphasic and can still reveal his emotions by the expressive movements, his fruitless attempts are accompanied by exclamations of discontent and vexation, with the expressive movements of despair, shame or anger, not unlike the behavior of a normal person after a long struggle to solve a mechanical puzzle. Now and then a patient, after prolonged floundering, will suddenly and unexpectedly succeed; but if he try the same movement again a little later on, he meets with as many difficulties as at first.

An excellent test for apraxia is to ask the patient first to imitate the movement of grinding coffee in a coffee-mill, and, immediately afterward, to turn the handle of a hand-organ. This test has been called by Heilbronner the shibboleth of apraxia-testing. Even in mild apraxia,

where each of these two movements by itself may be satisfactorily performed, the successive performance is faulty, resulting in a compromise between the two movements resembling an unskillful attempt at sawing wood.

It is much harder, as a rule, for the patient to perform a movement entirely from memory on request than to deal with the natural objects before him, though the movements under the latter conditions should also be tested. We can ask him to open a lock with a key, to take money out of a purse, to open a pen-knife, to light a safety-match on its box, to seal a letter, to affix a postage stamp, to sew, to knit, or to play a musical instrument.

In some cases apraxic disturbances appear on attempts at imitation of movement. We may passively move a non-apraxic extremity and ask the patient to imitate the movement with the apraxic extremity, or we may make movements before him ourselves, and ask him to imitate them, standing either symmetrically with him, or, to make the test more difficult, facing him.

Apraxia is most common in the upper extremities and may affect one or both. The most frequent combination met with is right hemiplegia with left-sided dyspraxia. A few cases of unilateral apraxia without paralysis of the opposite side have been described. Apraxic disturbances in the lower extremities are known, but have been as yet little studied.

Apraxic disturbances of the trunk have also been described; the patients had difficulty in turning over in bed, in sitting down upon and rising from a chair. Care must of course be taken not to confuse apraxia with ataxia in such cases. Bilateral apraxia of the muscles of the face and head manifest themselves by inability to blow or to whistle.

In severe apraxic states the patient may find it difficult or impossible to take a drink of water or to feed himself. He may bite at the glass or spoon, or make bizarre movements of the tongue, or be unable to hold the glass and bring it to his mouth.

Obviously these disturbances of the more complicated movements of the extremities, face and trunk run closely parallel to the disturbances of movement described in aphasia and agraphia; indeed, aphasic and apraxic disturbances belong together in systematic description. Aphasia and agraphia are, in reality, apraxia in the domain of the speech and writing movements.

### (3) *Confusions of Movements in Apraxia*

Just as in aphasics we distinguish between verbal paraphasia or word-confusion and literal paraphasia or word-distortion, so in apraxia we distinguish between confusion of movements and the distortion of movements above described.

When movements are confused, the attempt to make one movement results in the performance of another different movement, usually due to perseveration, the movement resulting being identical with or resembling a movement performed earlier. Sometimes a part of the movement only will show this perseveratory tendency. Such movement confusions are best seen on attempts to manipulate objects; instead of making the movement intended, the patient may seize the object in a convulsive way and temporarily be unable to release it, his mistake leading him to attempts forcibly to shake the object out of his hand. Or, instead of manipulating the object intended he may take another. Sometimes while lying in bed such a patient will seize the coverlet and be unable to let go of it. Heilbronner describes a patient who captured his own thumb in the hollow of his hand and could not let it go.

The separation of the apraxic limb from the will and the personality of the patient is a striking feature, and the patients themselves notice this and complain of it. A patient will often threaten his left hand with his right, saying he cannot trust his left hand; it will not do what he tells it to do. Such patients describe the actions of the apraxic hand, not as their own, but as those of *the* hand, or they may speak of it as belonging to a third person; "now he is doing that."

Very peculiar confusions of movement are sometimes met with. On the way to performance of a given movement the intention seems to become "switched off"; a man starting to comb his hair will stick the comb behind his ear as though it were a pen, or, beginning to peel an apple, will suddenly cut it through the middle, or, on attempting to blow a wind-instrument, will try to smoke it, or, on taking hold of a lead-pencil for writing, will stick it in the ink-bottle, or, instead of putting on his trousers in the ordinary way, will attempt to use them as a coat. One of Heilbronner's patients tried to peel a hard-boiled egg like an apple. The analogy to the verbal paraphasias is obvious.

In a systematic examination of an apraxic disturbance, the following routine may be followed:

(1) Can the patient move parts of his body without applying force to any external object? (Wrinkle nose, show tongue, make a fist, spread the fingers, cross the knees.)

(2) Can the patient perform automatic symbolic acts? (Winking, shaking hands, kissing, taking an oath, saluting, beckoning.)

(3) Can the patient apply his movements properly when asked to use external objects? (Lighting a cigar, pouring water into a glass, affixing a postage stamp, opening a pen-knife.)

(4) Can he make purposeful movements (in the absence of the external object), that is to say, can he reproduce the movements from memory? (Grind a coffee-mill, turn a hand-organ, catch a fly, count out money, lead an orchestra.)

(5) Can he perform purposeful movements on his own body? (Brush the teeth, blow the nose, pull an ear, wipe an eye, scratch himself.)

(6) When simple and complicated movements such as those above described are made by the examiner in front of the patient, can he imitate them?

(7) How does the patient behave when spontaneously handling objects?

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*Also:* ***1906,*** *xix, 217–243.*

## (*b*) *Peculiarities of Conduct Met With in Abnormal Mental States*

### i. Motor Agitation

By *motor agitation* or excitation is meant a state in which voluntary acts are performed in increased numbers and very rapidly. Movements appear to be easy for the patient; normal inhibitions are removed; there seems to be no sense of fatigue. The highest grade of motor agitation is met with in *maniacal excitement* (*e. g.,* in manic-depressive insanity, in dementia paralytica, in the episodic maniacal states of dementia praecox, paranoia and epileptic insanity).

### ii. Motor Stupor and Aboulia

By *motor stupor,* or *aboulia,* is meant the pathological weakness of will in which motor discharges are interfered with by abnormally intense inhibitory processes.

Certain special perversions of voluntary activity are met with in disease. Among them may be mentioned (1) stereotyped movements and attitudes, (2) command-automatisms, and (3) impulsive acts.

### iii. Stereotyped Movements and Postures

The patients may assume uncomfortable attitudes and maintain them for long periods (*stereotyped postures*). They often resist both passive change of posture and request for active change thereof (*negativism*).

Other patients repeat monotonous, often rhythmical, movements over and over again (*stereotyped movements*). This frequent repetition of the same movement is sometimes called *motor perseveration.*

### iv. Command-automatism

By command-automatism is meant an abnormal suggestibility to movement. Thus, a patient may repeat movements made before him (*echokinesis* or *echopraxia*), or may repeat words pronounced before him (*echolalia*). The stereotyped repetition of a movement at command is closely related to these phenomena.

If the limbs be placed in a given position this may be maintained for a long time, as in *waxy flexibility* and in *catalepsy.*

Fig. 557.—Catalepsy. (Med. Service, J. H. H.)

### v. Impulsive Acts or Deeds

By impulsive acts or deeds we mean voluntary movements that the patient performs as the result of a temporary psychomotor overvaluation. They may be due (1) to intense affective disturbances (*e. g.,* anger, anxiety, pathological libido), (2) to imperative ideas, or (3) to delusions.

For a fuller discussion of disturbances of will, and of other psychiatric phenomena, the reader may consult my article in the last volume of Osler and McCrae's "Modern Medicine," or one of the modern text-books of psychiatry (see References).

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# F. Certain Special Examinations Bearing upon the Condition of the Nervous System

Under this caption will be considered:

1. The external examination of the head and measurements of the head and body.
2. X-ray examinations of the central nervous system, skull and spine.
3. Lumbar puncture, and puncture of the ventricles of the brain.
4. Electrodiagnosis and electroprognosis.

## 1. External Examination of the Head, and Measurements of the Head and Body

### (a) *Inspection and Palpation*

On inspection and palpation of the skull, information is obtained regarding its form. It should be inspected from in front, from behind and from each side. We pay attention especially to the mode of junction of the skull-capsule with the facial skull, the position of the root of the nose, the prominence of the supraorbital ridges, the distance apart of the frontal eminences and their prominence, the character of the temporal region on each side, the skull just above the ears, and the shape of the back of the head. Asymmetry (scars, exostoses, etc.) can often be best made out by palpation with the eyes shut. Before palpating, we place the tips of the fingers close together in a single horizontal plane (say on a table). With the fingers held in this position, they are allowed to glide slowly over the surface of the skull, when abnormalities in form, and especially

asymmetry, can be far better made out than by the index finger alone. The lines of the sutures should be especially palpated. In children the size of the fontanelles should be ascertained.

### (*b*) *Measurements of the Head* (*Cephalometry*)

For clinical purposes, measurements are made (1) with a metal centimeter-tape, for curves and circumferences, and (2) with Benedikt's graduated compasses for linear measurements.

#### i. Measurements of Curves and Circumferences

The following measurements should be made:

(1) Greatest anteroposterior curve (Nt), from the middle of the glabella (N) to a point (t), which lies 1.25 mm. higher than the lowest sharply definable point of the external occipital protuberance as palpated by the index finger of the left hand; in man Nt is about 35–37 cm.

(2) Horizontal circumference, measuring around the head over the end points (N and t) of the greatest anteroposterior curve; in man 49–55 cm.

(3) Greatest transverse frontal curve, measuring from the root of the zygoma (behind the jaw-joint) on one side, up over the skull and down to the root of the zygoma on the other side; in man 29–34 cm.

(4) Length of curve from glabella (N) to anterior end of sagittal suture ($\alpha$).

(5) Length of curve from glabella (N) to posterior end of sagittal suture ($\beta$).

(6) Length of sagittal suture ($= N\beta - N\alpha$).

#### ii. Linear Measurements (Compass)

(1) Greatest length (L) in the median plane, forehead to most posterior point of occiput; in man 16.5–19.0 cm.

(2) Greatest breadth (Br), or linear distance between the points most lateralward from the median plane on the two sides; in man 13.5–15.6 cm.

(3) The length-breadth index ($\frac{100\ Br}{L}$), known as L.-Br.-I. Thus are distinguished (a) the brachycephalic or short heads, (b) the dolichocephalic or long heads, and (c) the mesocephalic or orthocephalic heads (of medium length).

*International Skull Indices*

A. Dolichocephalic 55.5–74.9.
B. Mesocephalic 75.0–79.9.
C. Brachycephalic 80.0–99.9.

The L.-Br.-I. for the head is greater than for the naked skull. For full details of head- and body-measurements see the last edition of Vierordt's *Daten und Tabellen für Mediziner.*

Very large heads (macrocephalic) and very small heads (microcephalic) are abnormal.

Marked depression between the facial skull and the cerebral skull; marked projection of the upper jaw (prognathia); or projection of the mandible so that the lower row of teeth project beyond the upper, should be especially noted. In this connection v. Ihering's *profile-angle* may be measured; it is formed by the junction of two lines, (a) that from the middle of the external auditory canal to the lower margin of the bony orbit of the same side, and (b) that from the frontonasal junction to the most prominent point of the alveolar process of the maxilla of the same side. This angle measures (1) in orthognathia, 89–91°, (2) in prognathia, 76° or more, (3) in opisthognathia, 91° or more.

### (c) *Measurements of the Adult Body*

| | Average Statistics of Hoffmann | | Topinard's Percentages |
|---|---|---|---|
| | Men | Women | |
| Body-length | 167.8 | 156.5 | 100 |
| Trunk-length (vertex to perineum) | 98.5 | 93.7 | 52.5 |
| Height of head (vertex to angle of mandible) | 18.5 | 17.4 | 13.3 |
| Length of neck (occiput to 7th cervical spine) | 24.6 | 23.4 | 4.2 |
| Distance from 7th cervical spine to perineum | 61.6 | 58.2 | 35.0 |
| Lower extremity (crista ilii to sole of foot) | 103.0 | 98.4 | 47.5 |
| Upper extremity (shoulder to tip of middle finger) | 74.2 | 69.2 | 45.0 |
| Shoulder-breadth | 39.1 | 35.2 | 23.0 |
| Hip-breadth (iliac crest to iliac crest) | 30.5 | 31.4 | 18.8 |
| *Parts of Extremities* | | | |
| Upper arm | 31.2–32 | 29 –30 | 19.5 |
| Forearm | 24.6–27 | 22.8–24 | 14.0 |
| Hand | 18.4–20 | 17.4–18 | 11.5 |
| Trochanter to sole | 89.8 | 84.8 | .... |
| Thigh (trochanter to knee) | 41.9–43 | 39.8 (37) | 20 |
| Leg (knee to ankle) | 39.6–43 | 37.8 (36) | 23 |
| Foot-height (lat. malleolus to sole) | 7.8 | 7.8 | 4.5 |
| *Certain Other Dimensions (Krause)* | | | |
| Total height | 173.4 | 162.6 | 100 |
| Vertex to navel | 69 | 65 | 40 |
| Navel to symphysis | 14 | 16 | .... |
| Navel to sole of foot | ..... | ..... | 60 |
| Circumference of trunk at iliac crest | 81 | 84 | .... |
| Distance between trochanters | 34 | 35 | .... |
| Width of hand at middle | 11 | 9 | 6 |
| Length of foot (heel to toes) | 26 | 23 | 15 |

### (*d*) *Stigmata of Degeneration*

Of the hereditary stigmata sometimes indicating psychopathic or neuropathic inheritance, but sometimes due to simple local developmental anomalies, may be mentioned:

(a) Anomalies of the external ear.

(1) Absence or imperfect development of the lobule of the ear.
(2) Absence of the helix or antihelix.
(3) Large outstanding ears with low ridges and flat grooves (Morel's ear).
(4) Marked Darwinian tubercles.
(5) Markedly projecting antihelix (Wildermuth's ear).

(b) Other developmental anomalies. These include harelip, cleft palate, arched hard palate, anomalies of dentition, retinitis pigmentosa, albinism, congenital coloboma, eccentric pupils, polydactyly, syndactyly, hypospadia and other congenital anomalies.

(c) Psychic stigmata of degeneration. These include:

1. Abnormal affective states, including:
   (a) Striking capriciousness of emotional life, with violent outbreaks of anger or outspoken anxiety.
   (b) Obstinate persistence in definite pathological moods (grouch; depression).
   (c) Marked tendency to syncopes, convulsive states, unmotived vomiting.
   (d) Faulty development of higher intellectual feelings (social, altruistic, esthetic), with abnormally great development of the egoistic feelings, including the sexual.

2. Abnormal disharmonious intellectual development, with dominance of the fantasy, or one-sided intellectual endowment (*e. g.*, unusual memory for language, mathematical faculty, musical talent), while conceptions and judgments in other intellectual domains are faulty. The psychasthenic phobias and obsessions belong here. Certain disturbances of sleep (*e. g.*, pavor nocturnus, protracted enuresis nocturna) are suggestive. Marked lack of tolerance to alcohol and tobacco are common signs.

### (*e*) *Percussion of the Skull*

Percussion of the skull is of some value for clinical diagnosis. Direct percussion with the finger is better than with a hammer. Increased sensitiveness on percussion, if sharply circumscribed, is highly important, often locating a focal lesion (tumor, abscess) in or near the cerebral cortex. Diffuse hyperesthesia of the skull is of no diagnostic value.

A tympanitic tone, or a cracked-pot sound, on percussion may indicate a thinning of the skull, due to a focal lesion (*e. g.*, tumor), to hydrocephalus, or to osteoporosis.

### (f) Auscultation of the Skull

Auscultation of the skull should not be omitted. Murmurs are heard in aneurisms of the basilar artery (back of head) and of the internal carotid artery (over temporal region). Murmurs are sometimes heard over vascular brain tumors.

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## 2. X-ray Examination of the Nervous System, the Skull and the Spine

X-ray examinations of the skull are occasionally helpful in diagnosis. The findings in sinus disease are described under the Respiratory Apparatus; those in mastoid disease are becoming equally important. Malformations of the skull and spine, cervical ribs, abnormalities of the bones of the extremities in organic nervous diseases, can often be detected by

x-ray examinations. Enlargement of the sella turcica can often be clearly made out in cysts and tumors of the hypophysis. Certain foreign bodies in the skull and spine or in the brain and cord can be made out; thus bullets, knife-tips and grains of shot yield sharp pictures and can be exactly localized. Tumors of the bones of the skull and tumors or caries

Fig. 558.—Calcified Pineal Gland. (X-ray Dept., J. H. H.)

of the spine can be recognized in x-ray plates. Tumors of the brain itself are visible only when calcified. A calcified pineal gland is sometimes observable.

When signs of root-lesion of the spinal nerves exist, x-ray plates should always be made, since the nerve roots may be involved in some process affecting the bones of the spine (arthropathies, caries, carcinosis, dislocation, fracture, etc.).

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## 3. Lumbar Puncture and Examination of Cerebrospinal Fluid

Lumbar puncture and examinations of the cerebrospinal fluid have already been described (see Exploratory Punctures).

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NOTE.—See also references on Lumbar Puncture in Part III.

## 4. Cerebral Puncture through the Skull (Method of Neisser and Pollak)

The head is shaved and the skin disinfected and anesthetized with ethyl chlorid. The soft parts and skull are perforated quickly by a rapidly rotating auger 2 mm. in diameter, driven by an electromotor, care being taken to stop the rotation and to withdraw the auger at the moment the feeling of resistance ceases, when the lamina interna is perforated. Through the channel thus made, a needle 7 cm. long (carrying a centimeter scale), attached to a syringe, is introduced. One tests first for the presence of extradural fluid. If none is obtained, the needle is shoved through the dura, a vacuum being maintained in the syringe as it proceeds gradually into the depth. The method has been employed as an aid in the diagnosis of cerebral abscess, cerebral hemorrhage, brain tumors and hydrocephalus. After the needle has been removed the opening is closed with a sterile dressing.

The part of the skull punctured will depend upon the nature of the pathological process suspected, but, in every case, precautions should be taken to avoid arteries, veins, and the sinuses. Temporal abscesses are usually sought by puncture 0.5-0.75 cm. perpendicularly above the upper attachment of the external ear. For further details the directions of Neisser and Pollak should be consulted.

This method is of very doubtful value. On occasions when it would be resorted to it is usually wiser to open the skull by a decompression operation, and then explore with a needle.

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## 5. Electrodiagnosis and Electroprognosis

In electrical examinations of the muscles, both forms of current, (1) the faradic or interrupting, and (2) the galvanic or constant current, are employed. The "indifferent" pole or large flat electrode (70 cm.$^2$), is applied over the sternum or the back of the neck, the "different" pole or stimulating electrode to the muscle or nerve to be examined. For the latter, a small electrode is used (3 cm.$^2$ for nerves, 10 cm.$^2$ for direct stimulation of the muscle) in order that the current may reach the point to be irritated in the greatest possible density.

As is well known, the density (D) increases as the transverse diameter (T) of the electrode diminishes and as the intensity of the current (I) increases; thus $D = \frac{I}{T}$.

On applying the electrodes, they should be moistened thoroughly with warm water, or warm salt solution, in order to diminish the resistance to conduction as much as possible.

### (a) *The Faradic Current*

In making examinations with the faradic current, to test the so-called *faradic excitability,* it is of course the secondary or induced current that is used, and we express the strength of the current required to cause minimal but distinct contraction (tetanus) by recording the distance in millimeters to which the secondary coil has to be pulled out. The further apart the two coils are, the weaker the current. The strength of the faradic current can also be varied by pulling the iron core of the primary coil in and out. The further in the core, the stronger is the current, the further out, the feebler. The stimulating electrode may be applied over a motor nerve (indirect stimulation of the muscle) or over the muscle itself (direct stimulation).

On stimulating a given nerve, it is important to notice whether or not all the muscles supplied by it respond; any muscle failing to respond to indirect faradic stimulation should be carefully tested by direct stimulation.

### (*b*) *The Galvanic Current*

In testing with the galvanic current for *galvanic excitability* we can stimulate in four different ways, according as we excite with the cathode or the anode, and, in each instance, as we close or open the circuit; the four stimuli are then (1) cathodal closure, (2) cathodal opening, (3) anodal closure, (4) anodal opening. We first apply the negative pole, or cathode, to the nerve or muscle to be tested and begin by using the cathodal-closure stimulus.

If one is in any doubt as to which is the anode and which the cathode, he may immerse the ends of the conducting wires in water, when bubbles of hydrogen will appear at the cathode; or the wires may be immersed in a solution of potassium iodid and starch, when clouds of blue color will appear at the anode, owing to the setting free of iodin by the nascent oxygen.

We apply at first very feeble currents, gradually increasing the strength by means of the rheostat until we have reached the strength of current that calls forth a minimal contraction of the muscles at the moment when the current is closed (cathodal closure contraction, CaClC). The strength of current is read off on the galvanometer.

By means of a commutator, the stimulating electrode may now be changed from cathode to anode, and we next determine the amount of current necessary to cause a minimal contraction on closing the current (anodal closure contraction, AnClC). By the thumb on the interrupter, we cause closing or opening of the current at will. The electrodes are, of course, to be held steadily on the spot to be stimulated.

#### Examination by Means of Condensor Discharge.

Another method of electrical examination, sometimes employed, consists in charging an electrical condensor by a current the tension of which varies (as read off on the volt-meter) and then discharging this condensor through the body of the patient. The capacity of the condensor usually chosen is one mikrofarad.

Knowing (1) the capacity of the condensor and (2) the tension to which it is charged (in volts), the product of these two values gives (3) the amount of electricity (in mikrocoulombs) that is discharged through the body; in other words, the amount of electricity (Q) = capacity (C) multiplied by tension (V).

On using this condensor-method, extraordinarily brief impulses are employed and the time required for discharge is so short that no alterations of resistance or of excitability can occur. The method, as used clinically, has been described by Zanietowski.

### (*c*) *Normal Electrical Findings*

Under normal conditions the feeblest currents that are capable of causing a contraction do so on cathodal closure of the current; with somewhat stronger currents, this cathodal closure contraction becomes more marked, and anodal opening and anodal closure contractions begin

to appear. With still stronger currents, cathodal closure causes continuous contraction, or tetanus, while anodal opening and closure still give rise to a single contraction only. If one cautiously increase the intensity of the current still more, a point will be reached when cathodal opening of the current also causes contraction.

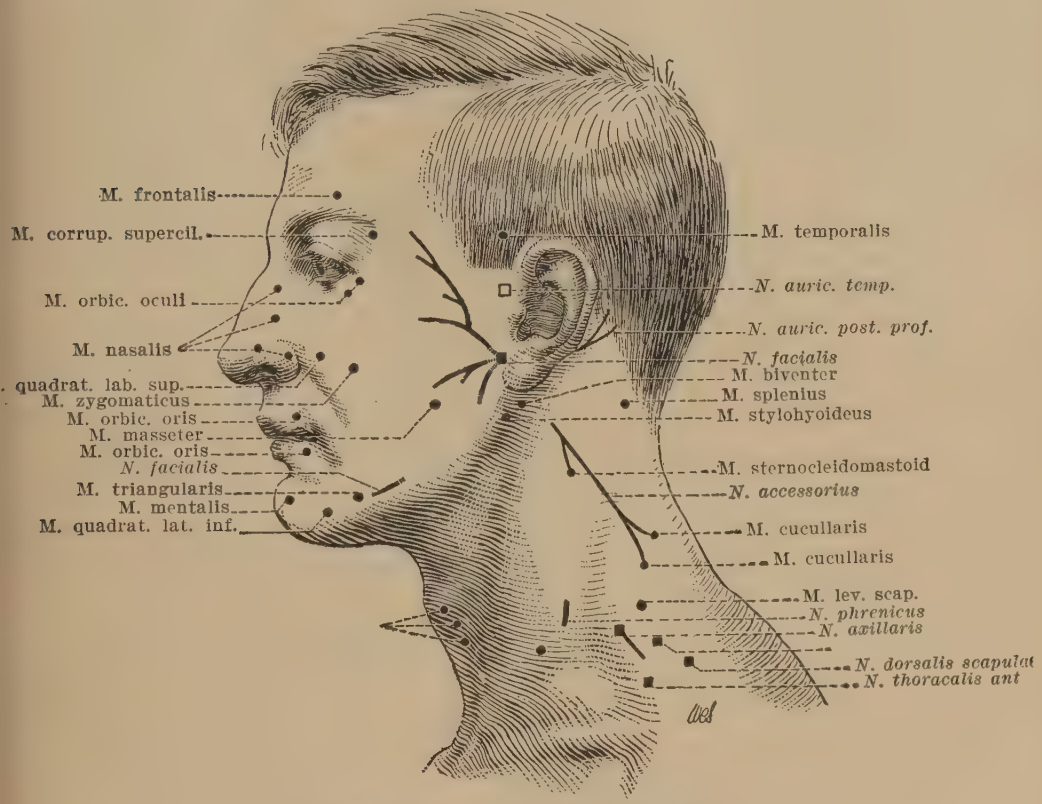


Fig. 559.—Motor Points of the Head and Neck.

The series of responses on electrical stimulation with currents gradually increasing in intensity under normal conditions are shown, therefore, in the following table:

1. Cathodal closure contraction: CaClC.
2. Anodal closure contraction: AnClC.
3. Anodal opening contraction: AnOC.
4. Cathodal closure tetanus: CaClTe.
5. Cathodal opening contraction: CaOC. The strength of current necessary to yield CaOC is usually so great (7–15 milliampères), that the test is as a rule not carried so far.

This normal series of responses holds for indirect stimulation of the muscles from the nerves; when the electrodes are applied directly to the muscles, responses occur chiefly on closure of the currents, the anodal

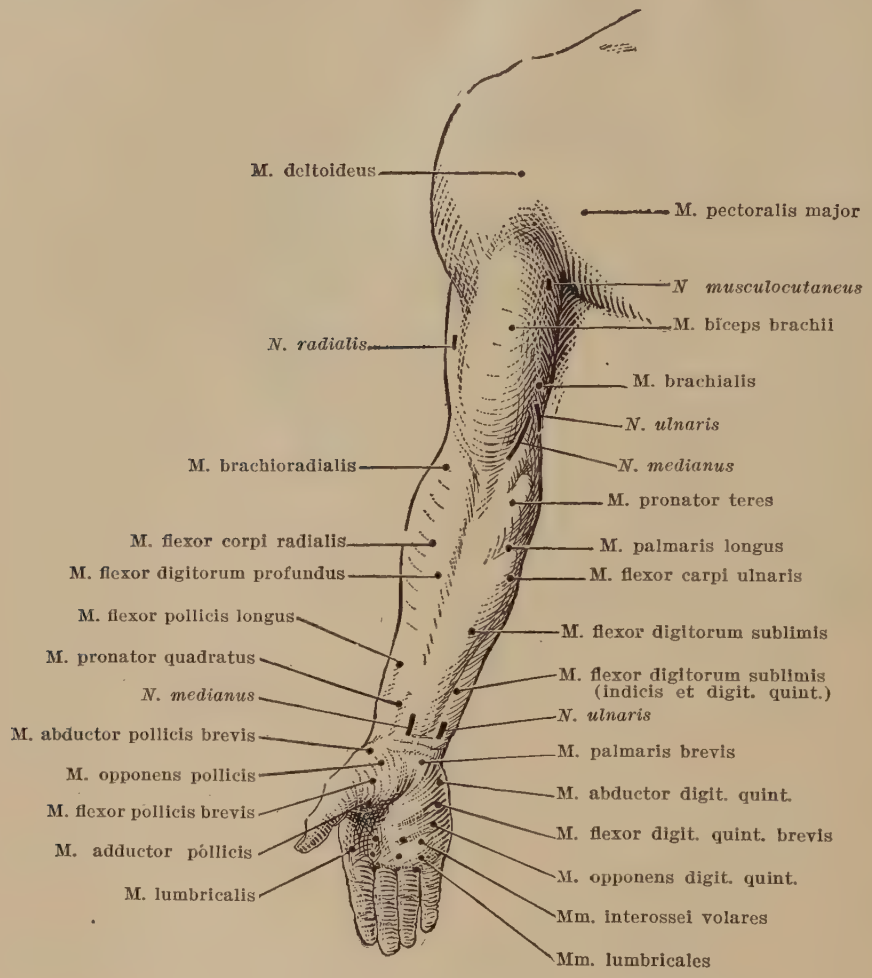


Fig. 560.—Motor Points of Upper Extremity. Anterior Surface.

closure contraction occurring with currents almost as feeble as those that excite a cathodal closure contraction.

We apply the stimulating electrodes to the so-called *motor points* (Erb). These are points on the skin where the motor nerves lie superficially, or near where the nerves enter the muscles.

The most important motor points are shown in the accompanying figures.

We place the patient in a good light in order to be able to see the slightest response of the muscle. A contraction can sometimes be felt when it is too feeble to be seen. The patient should be instructed to relax the muscles of the part undergoing examination. The examiner

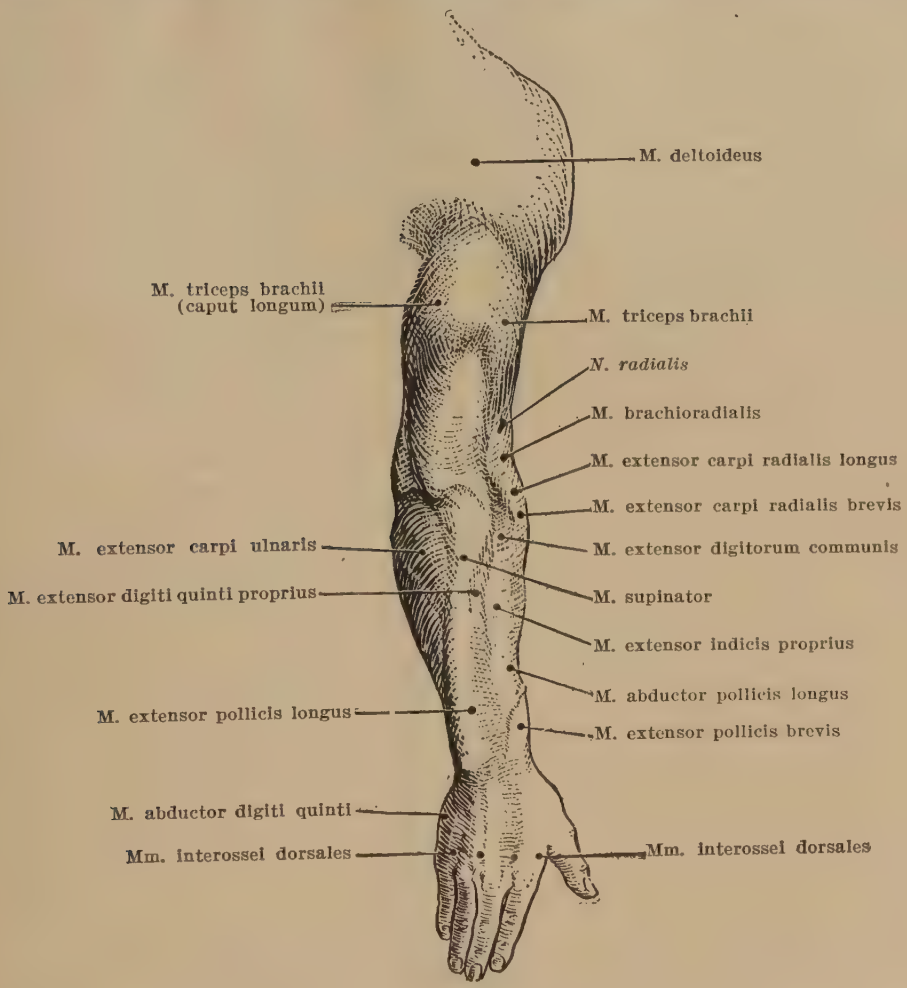


Fig. 561.—Motor Points of Upper Extremity. Posterior Surface.

should always test the strength of the current on his own skin before applying it to the patient.

It is rarely necessary to make a complete electrical examination of all the muscles of the body; this would be very time-consuming. The examination of a selected group of muscles in a suspected area usually suffices. One muscle tested carefully is often worth much more than a general examination made superficially.

On testing faradic reactions, we stimulate muscles always indirectly through their motor nerves, the individual muscles at the motor points, groups at the points corresponding to nerve trunks. On testing the muscles of an extremity, we place the parts in a position in which con-

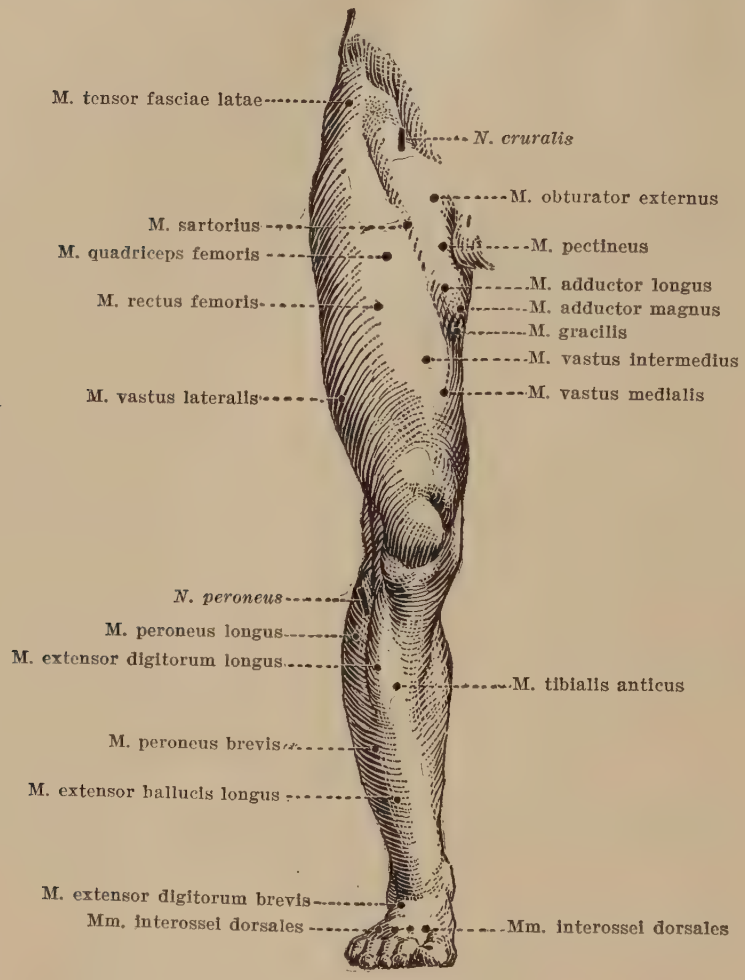


Fig. 562.—Motor Points of Lower Extremity. Anterior Surface.

tractions will become most evident, but we should not always expect a locomotor effect, and must often depend upon visible, or palpable, movement of the muscle beneath the skin.

Great difficulty is often experienced in making electrical tests on small children. It is difficult to keep them quiet, and, often, the extremities must be held

by someone during the examination; one must try to distinguish the contractions due to the electrical stimulation from voluntary contractions and reflex movements. The thick layer of fat in young children also obscures the results of the test.

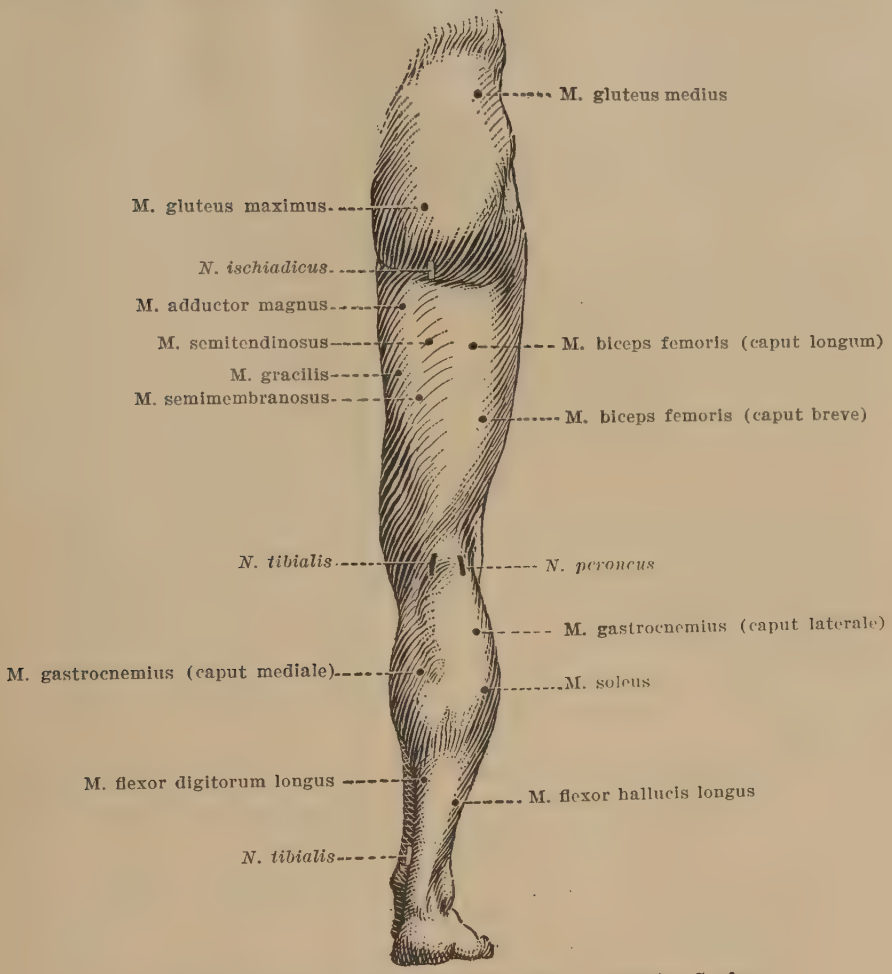


Fig. 563.—Motor Points of Lower Extremity. Posterior Surface.

### (*d*) *Disturbances of Electrical Excitability*

Pathological modifications in electrical excitability may consist, (1) in a quantitative change (increase or decrease), or (2) in both a quantitative and a qualitative change (reaction of degeneration).

#### i. Quantitative Changes in Excitability

Electrical excitability may be increased or diminished either for the faradic or for the galvanic current.

In judging of quantitative changes of excitability to the faradic current, one must be acquainted with his instrument and know the approximate coil-distance that elicits responses under normal conditions. Only very marked deviations from this distance should be regarded as pathological; no attention should be paid to slight differences. In unilateral affections, the healthy side may be contrasted with the diseased side. For quick orientation one may test a few points: (1) N. frontalis, (2) N. accessorius, (3) N. ulnaris, (4) N. peroneus.

On testing the galvanic excitability quantitatively, we read off the amount of current in milliampères on the galvanometer. As is well known, most of the motor points respond on cathodal closure to a current of 0.5 to 2–5 milliampères. Exact figures for the different points as tested by a definite instrumentarium are available in the following tables of Stintzing:

Scale of Faradic Excitability of the Nerves
(Coil-Distance in Millimeters)

| | | Upper Limit | Lower Limit | Average |
|---|---|---|---|---|
| 1 | N. accessorius | 130 | 145 | 137.5 |
| 2 | N. musculocutaneus | 125 | 145 | 135 |
| 3 | R. mentalis | 125 | 140 | 132.5 |
| 4 | N. ulnaris I | 120 | 140 | 130 |
| 5 | R. frontalis | 120 | 137 | 128.5 |
| 6 | R. zygomaticus | 115 | 135 | 125 |
| 7 | N. medianus | 110 | 135 | 122.5 |
| 8 | N. facialis | 110 | 132 | 121 |
| 9 | N. ulnaris II | 107 | 130 | 118.5 |
| 10 | N. peroneus | 103 | 127 | 115 |
| 11 | N. cruralis | 103 | 120 | 111.5 |
| 12 | N. tibialis | 95 | 120 | 107.5 |
| 13 | N. radialis | 80 | 120 | 105 |

Scale of Galvanic Excitability of the Nerves
(Milliampères for CaClC)

| | | Upper Limit | Lower Limit | Average |
|---|---|---|---|---|
| 1 | N. musculocutaneus | 0.28 | 0.05 | 0.17 |
| 2 | N. accessorius | 0.44 | 0.10 | 0.27 |
| 3 | N. ulnaris I | 0.9 | 0.2 | 0.55 |
| 4 | N. medianus | 1.5 | 0.3 | 0.9 |
| 5 | R. mentalis | 1.4 | 0.5 | 0.95 |
| 6 | N. cruralis | 1.7 | 0.4 | 1.05 |
| 7 | N. peroneus | 2 | 0.2 | 1.1 |
| 8 | R. zygomaticus | 2 | 0.8 | 1.4 |
| 9 | R. frontalis | 2 | 0.9 | 1.45 |
| 10 | N. tibialis | 2.5 | 0.4 | 1.45 |
| 11 | N. ulnaris II | 2.6 | 0.6 | 1.6 |
| 12 | N. facialis | 2.5 | 1.0 | 1.75 |
| 13 | N. radialis | 2.7 | 0.9 | 1.8 |

**Increased excitability** is seen in tetany, where very feeble currents, wholly without effect in healthy persons, cause muscular contractions. A

similar hyperexcitability is seen after lightning-stroke. In the so-called *neurotonic reaction,* found sometimes in hysteria (Marina), and in progressive muscular atrophy (Remak), though there is no increase of the quantitative minimum irritability, anodal opening contraction appears very early from stimulation of the nerve but not of the muscle. There is also a special tendency to tetanus on stimulation of the nerve at cathodal closure and at anodal opening.

A simple **diminution of excitability** may be met with in long-standing paralysis not accompanied by degenerative atrophy of the muscles (*e. g.,* upper motor neuron paralyses, arthritic muscular atrophies and the various myopathies).

### ii. Qualitative Changes in the Reactions (Reaction of Degeneration)

For diagnostic purposes this is the most important form of change in electrical excitability. The reaction of degeneration is usually abbreviated as *DeR.* It may practically always be considered as a sign of degenerative atrophy of the muscle due to disease or destruction of some part of the lower motor neuron (anterior horn cell, ventral root, peripheral nerve, or nerve-ending in muscle).

The *reaction of degeneration* may be complete or partial.

The *complete DeR* is characterized by (1) loss of excitability of nerve to the faradic current; (2) loss of excitability of muscle to the faradic current; (3) loss of excitability of nerve to the galvanic current; (4) increase of excitability of muscle to the galvanic current and modification of the response thereto, in that the contraction is sluggish and wormlike, and that the contraction on anodal closure (AnClC) is greater than the contraction on cathodal closure (CaClC); thus AnClC > CaClC. The increase of the galvanic excitability is present only in the early stages; later it grows less, until, finally, a feeble, wormlike contraction on powerful stimulation at anodal closure is all that is left. Far more characteristic than predominance of the anodal closure contraction over the cathodal closure contraction (for the two may be equal), is the *sluggish, wormlike nature of the contraction,* which is pathognomonic.

In the *partial DeR,* the excitability of the nerves (both faradic and galvanic) may be only diminished; the faradic excitability of the muscles is diminished or lost; on direct galvanic stimulation of the muscle, the slow, wormlike contraction appears, and the contraction-formula may be reversed, so that AnClC is greater than CaClC. Every gradation is met with between such a partial DeR and the complete DeR described above. The milder forms of DeR are easily overlooked, but will usually be recognized if the examiner keeps his attention focused upon the sluggish, wormlike character of the muscular contraction as compared with the normal response.

After experimental section of a nerve, or after injury or disease,

the DeR does not appear immediately; about a week elapses before it is fully present. The course of irritability in different forms of lesion of the lower motor neurons is graphically shown in the well-known curves of Erb (see Special Texts).

The DeR, once it has appeared, persists, unless, through regeneration of the lower motor neurons, a normal condition is reëstablished. During nerve regeneration, voluntary power over the muscle may reappear some time before normal response to electrical stimulation returns.

In the so-called *mixed DeR,* some fibers of a muscle retain their normal reactions, while adjacent fibers show DeR; this is due to involvement of certain only of the nerve fibers and muscle fibers in the degenerative process (*e. g.,* progressive muscular atrophy).

The DeR is the most constant and certain sign of true degenerative processes in the lower motor neurons and the muscles they innervate. It is present in all serious lesions (a) of the nerves containing motor axons, (b) of the anterior horns of the spinal cord, and (c) of the anterior roots of the spinal nerves; indeed, it occurs in all diseases affecting the lower motor neurons in any of their parts (cell-body, axons, terminals).

Among these processes may be mentioned the following:

I. Diseases affecting the *cell-bodies* of the lower motor neurons.
   - A. Spinal.
     - (1) Poliomyelitis anterior.
     - (2) Amyotrophic lateral sclerosis.
     - (3) Progressive muscular atrophy.
     - (4) Gliosis spinalis, affecting anterior horns.
     - (5) Forms of myelitis affecting anterior horns.
   - B. Bulbar.
     - (1) True bulbar paralysis.
     - (2) Polioencephalitis inferior.

II. Diseases affecting the *axons* of the lower motor neurons.
   - A. Axons of anterior roots of spinal nerves, or of roots of motor cerebral nerves.
     - (1) Compression by neoplasms.
     - (2) Meningeal thickenings (*e. g.,* lues, pachymeningitis cervicalis hypertrophica).
     - (3) Compression at intervertebral foramina in diseases of the spine (caries, fracture, dislocation, tumor).
   - B. Severe lesions of axons in their course toward the periphery.
     - (1) Traumatic.
     - (2) Toxic and infectious.
       - (a) Rheumatic (*e. g.,* facial paralysis).
       - (b) Lead-palsy.
       - (c) Alcoholic neuritis.
       - (d) Arsenical neuritis.
       - (e) Polyneuritis infectiosa.

### iii. Certain Special Types of Abnormal Electrical Reaction

In certain diseases, peculiarities of electrical response are met with. Among these, the two most important are: (1) myotonic reaction, and (2) myasthenic reaction.

#### (1) *Myotonic Reaction of Erb (MyR).*

In Thomsen's disease (myotonia congenita), a peculiar form of response to electrical excitation is met with. There is very little change in the faradic excitability of the nerves; the stimulation of the nerves with stronger currents causes a tonic contraction of the muscles with persistence of the contraction after stimulation, while single opening induction-stimuli cause only a brief contraction. The direct faradic muscular irritability is increased; even feeble currents cause a tonic contraction with long persistence. On continuous faradic stimulation, one sometimes sees an undulation of the muscles stimulated.

Galvanic excitability of the nerves is somewhat depressed. The direct galvanic muscular irritability is increased, but only closure contractions occur and usually AnClC is greater than CaClC. The striking feature is the slow, tonic character of the muscular contractions and their persistence. By steady application of the galvanic current, a rhythmical undulation of the muscle occurs, a contraction-wave passing from the cathode toward the anode with stronger currents. This myotonic reaction is also observable in some normal animals (new-born mammals, normal toads) and in muscles after certain intoxications (digitalin, veratrin, oxalic acid, etc.).

#### (2) *Myasthenic Reaction of Jolly*

In myasthenia gravis, if a tetanizing faradic current be applied, either to nerve or muscle, and repeated at intervals of a second, the muscular contractions grow feebler with every stimulation until they finally disappear, though the muscle, after a brief period of rest, may again show its normal excitability. Or, if one allow the current to act continuously for from 15 to 60 seconds, one will observe an even diminution of the contraction, which will, sooner or later, according to the strength of the stimulus, disappear entirely; here, also, a pause of less than a minute suffices to restore the muscle so that the stimulus becomes as active as before. A pause of a couple of seconds may be long enough to restore excitability of an exhausted muscle, and a muscle fatigued by the faradic current may still respond to the galvanic.

### (e) *Hints for Prognosis from Electrical Examination*

Considered along with other facts, the condition of electrical excitability may be of great importance for prognosis. This is well seen in

rheumatic facial paralysis (Bell's palsy), and in acute anterior poliomyelitis (infantile spinal paralysis).

In Bell's palsy, if DeR is still present after two weeks, we can be sure that at least several months or even a year will elapse before complete recovery, if recovery is to take place at all. If, on the other hand, at the end of two weeks, there is no marked DeR present, the lesion has been slight, and recovery may occur in a few weeks. If the DeR be partial, recovery may require 8 to 10 weeks. Furthermore, the course of the electrical changes during convalescence is helpful for prognosis; thus, if there be no return of mobility and no change in the DeR after 30 weeks, the prognosis is grave, whereas a gradual improvement in the electrical reactions is favorable.

In poliomyelitis anterior, if no DeR appear within 2 or 3 weeks, we can be sure that the anterior horn cells have been injured only slightly, but if the DeR become outspoken, the outlook for the paralyzed muscles is bad.

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## 6. Mechanical Excitability of Nerves and Muscles

A blow on a muscle with a percussion hammer usually calls forth a contraction in normal muscle, characterized by a quick contraction of the longitudinal bundles lying at the spot irritated and in the formation of a visible muscle-ridge (idiomuscular contraction). This mechanical excitability is increased in cachectic states (*e. g.,* anemia, neoplasm) and in all conditions in which the electrical DeR with increased galvanic excitability is present in the muscles. In the latter case, the response is not lightninglike but wormlike. There is also an increase in the excitability in myotonia congenita (Thomsen's disease). Mechanical excitability of the nerves is an important diagnostic sign in tetany. Thus, on tapping the skin over the facial nerve, or sometimes even on gentle stroking of the cheek, lightninglike muscular contractions occur (*Chvostek's phenomenon*). In less marked cases a slight blow with a percussion hammer below the zygomatic process will evoke a contraction at the angle of the mouth and within the nose on the same side. Pressure on the trunks of the nerves (with a blood-pressure apparatus, or with the fingers) will, in tetany, call forth tonic spasm in the forearm with the hand in the obstetrical position (*Trousseau's phenomenon*). Sometimes the sensory nerves are also hypersensitive to mechanical stimulation, so that a slight blow at one of Valleix's points will cause intense pain or paresthesia in the distribution of the nerve (*Hoffmann's symptom.*)

# Part XII

SECTION II

## UTILIZATION OF ACCUMULATED NEUROLOGICAL DATA FOR DECIDING UPON THE SITE OF THE LESION (LOCALIZING DIAGNOSIS, TOPICAL DIAGNOSIS)

## A. Introduction

After collecting data concerning the various functions of the nervous system according to the plan outlined in the preceding section, one has to value them (1) for a decision regarding the localization of the disease in the nervous system, and (2) for a decision regarding the exact nature of the pathological process that has been the cause.

The present section deals with the facts that help in locating the site of a lesion (Topical Diagnosis); while the following section will take up the diagnosis of the nature of the lesions (Special Diagnosis).

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### 1. Distribution of the Neuron Systems and of the Conduction Paths within the Nervous System

For topical diagnosis, a knowledge of the distribution of the many neuron systems and of the principal conduction paths in the peripheral and central nervous system is essential. Anatomists have, it is true, given us information regarding a great number of conduction paths (neuron chains) that as yet we are unable to use in our practical clinical work. But clinicians must be acquainted with those more important conduction paths injury to which gives rise to specific disturbances of neural function that we can recognize and therefore locate. The student, before

approaching this part of the subject, will then do well to refresh his memory by consultation of some good Anatomy of the Nervous System (see References) regarding the following paths:

*A.* *The afferent (sensory) paths.*
These include (1) the somesthetic path from the periphery through the lemniscus to the cerebral cortex; also the spinocerebellar paths and the spinothalamic paths; (2) the gustatory paths; (3) the vestibular paths; (4) the cochlear paths; (5) the optic paths; and (6) the olfactory paths.

*B.* *The efferent (motor) paths.*
These include (1) the lower motor neurons; (2) the upper motor neurons (pyramidal tracts); (3) the subcorticospinal paths (rubrospinal, thalamospinal, tectospinal, and vestibulospinal).

*C.* *The paths underlying the chief reflexes (including tonus).*

*D.* *The autonomic paths.*
These include the paths of the sympathetic and the parasympathetic systems.

*E.* *The higher associative paths.*
These include the paths concerned in aphasia, agnosia, and apraxia.

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[Note.—For other references see p. 125.]

## 2. The Larger Subdivisions of the Nervous System

While the most logical subdivision of the nervous system, anatomically and physiologically, is the subdivision, as above, into neuron groups and chains of neuron systems along functional lines, it is also convenient, clinically, to follow that rougher, older, anatomical subdivision into (1) peripheral nerves (Nn. spinales et cerebrales), (2) the spinal cord (*medulla spinalis*), (3) medulla and pons (*rhombencephalon,* including the *medulla oblongata,* and the *pons Varolii*), (4) the *cerebrum,* including (a) the midbrain (*mesencephalon*), (b) the interbrain (*diencephalon*), and (c) the end-brain (*telencephalon*), and (5) the *cerebellum* (strictly speaking, this belongs to the rhombencephalon). In our discussion of topical diagnosis we shall, therefore, begin with the criteria that permit us to localize lesions in the peripheral nerves and then go on to the criteria that permit of a localization in the spinal cord and in the higher parts of the nervous system.

# B. Diagnosis of Lesions of the Peripheral Nerves

Here we include the diseases of:

1. The cerebrospinal nerves; and
2. The autonomic nerves.

## 1. Diseases of the Cerebrospinal Nerves

The cerebrospinal nerves include (1) the spinal nerves (*Nn. spinales*), and (2) the cerebral nerves (*Nn. cerebrales*).

### (*a*) *Diseases of the Spinal Nerves* (*Nn. spinales*)

There are 31 pairs of spinal nerves; 8 pairs of cervical nerves (*Nn. cervicales,* $C_1$-$C_8$); 12 pairs of thoracic nerves (*Nn. thoracales,* $T_1$-$T_{12}$); 5 pairs of lumbar nerves (*Nn. lumbales,* $L_1$-$L_5$); 5 pairs of sacral nerves (*Nn. sacrales,* $S_1$-$S_5$); 1 pair of coccygeal nerves (*N. coccygeus*).

Each *spinal nerve* is formed of a motor (anterior) and a sensory (posterior) root, the latter having a special ganglion upon it. These *two roots* unite to form the main trunk of the spinal nerve, which, almost immediately, divides into an anterior part and a posterior part, each carrying motor and sensory fibers. The posterior branches, smaller than the anterior, supply the skin and muscles of the neck and back. The larger anterior branches unite to form several plexuses:

1. The cervical plexus (*plexus cervicalis*) ($C_1$-$C_4$).
2. The brachial plexus (*plexus brachialis*) ($C_5$-$C_8$, and part of $T_1$).

(The other thoracic nerves do not enter into the formation of plexuses.)

3. The lumbar plexus (*plexus lumbalis*), made up of $L_1$-$L_3$ and most of $L_4$.
4. The sacral plexus (*plexus sacralis*), made up of part of $L_4$ and $L_5$ and $S_1$-$S_4$.
5. The coccygeal plexus (*plexus coccygeus*), made up of a part of $S_4$ and of $S_5$, and the coccygeal nerve.

It will be noted that the diseases of the peripheral nerves include:

1. Those portions of the lower motor neurons that lie outside of the central nervous system; that is, all except their cell-bodies and dendrites and the proximal portions of their axons;
2. Those portions of the peripheral sensory neurons that lie out of the spinal cord and brain, including their cell-bodies (in the ganglia), their peripheral axons and their terminals, and the proximal portions of

their central axons, but not the main extent of the latter lying within the central nervous system (exogenous sensory fibers of the cord and brain). In lesions that affect the cell-bodies in the ganglia, the peripheral axons and the central axons will both be involved, since the ganglion cell is the trophic center of the peripheral sensory neuron. The sensory axons will then degenerate, not only in the posterior roots, but also within the central nervous system (posterior funiculi in the spinal cord, sensory fibers in the medulla and pons as far as the nuclei of termination of the cerebral sensory nerves).

Of the anomalies of function of the peripheral nerves we distinguish:

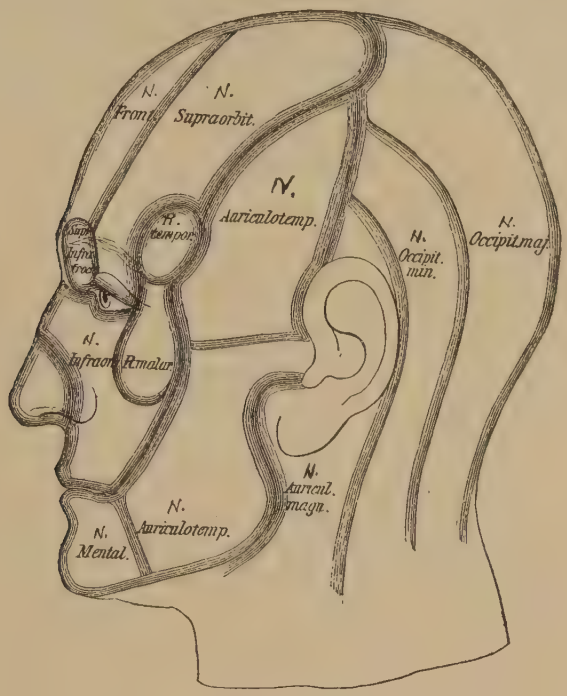


Fig. 564.—Areas Supplied by the Cutaneous Nerves of the Head. (After F. Merkel.)

1. Depression or abolition of conduction power, causing (a) *paralysis* in the domain of the motor nerves, and (b) *anesthesia* in the domain of the sensory nerves.

2. An irritative state: *spasms* in the domain of the motor nerves, and *pains* or *paresthesias* in the domain of the sensory nerves.

Since, further, the trophic center for the lower motor neurons and for the muscles they innervate lies in the cell-bodies of these neurons, any lesion of the peripheral motor nerves will cut off the muscles from their nutritive centers and so lead to degenerative atrophy with the characteristic electrical phenomena (See Electrodiagnosis).

From the grouping (topographical distribution) of the spasms or paralyses, on the one hand, or of the pains and anesthesia, on the other, we can decide, in the first place, whether the lesion has affected one nerve or several, and, in the second place, whether it is located in the nerve roots, in the plexuses or in the peripheral nerves distal from the plexuses.

Since localization according to nerve roots (as they emerge from or enter the spinal cord or brain) is of the greatest importance in connection with corresponding lesions of the spinal cord or brain stem, the distribution of symptoms corresponding to these nerve roots will be considered when the diseases of the spinal cord (segmental diagnosis) and of the medulla and pons are taken up.

Here we shall consider, therefore, the topographical distribution of the symptoms in lesions of the various plexuses and of the peripheral nerves (motor and sensory) distal from these plexuses.

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***Marie* (*P.*) & *Athanasio-Benisty, Mme.*** *L'individualité clinique des nerfs périphériques. Rev. neurol., Paris,* ***1914,*** *xxviii, 475–478.*

### i. Lesions of the Domain of the Cervical Plexus

According to the extent of the lesion, there will be variable combinations of sensory and motor symptoms in the domain of the four upper

cervical nerves. The most important nerve here is the *N. phrenicus,* which supplies the diaphragm. It may be injured in affections of the spinal column (fractures, caries, tumors) and of the meninges, or by compression or trauma in the neck or in the thorax; the phrenic nerve may also be involved alone or in combination with other nerves of the cervical plexus in infections and intoxications.

*Unilateral paralysis of the N. phrenicus* is easiest recognized, when suspected, by fluoroscopic examination of the diaphragmatic movements; one sees absence of movement of the diaphragm on inspiration on one side, or the diaphragm on that side lags behind the other. *Bilateral phrenic paralysis* causes severe clinical phenomena. Since the diaphragm is the chief muscle of inspiration, there is marked dyspnea, especially on exertion, and abdominal breathing is no longer possible; accordingly, only the upper part of the thorax expands and there is an absence of the normal bulging of the epigastrium on inspiration.

### ii. Lesions in the Domain of the Brachial Plexus

This plexus may be involved by: (1) tumors near the spine or in the supraclavicular fossa; (2) direct and indirect trauma; (3) injuries due to dislocations of the arm or fractures of the clavicle; (4) pressure from cervical ribs; (5) injuries to the new-born child during birth.

Three main types of lesion in the domain of the brachial plexus are recognizable: (1) the *upper lesion* of the brachial plexus (Erb's type); (2) the *lower lesion* of the brachial plexus (Klumpke's type); and (3) the *total lesion* of the brachial plexus.

#### (1) *Upper Lesion of the Brachial Plexus (Erb's Type)*

When the lesion affects the roots of $C_5$ and $C_6$ or the superficially-lying cord of the plexus formed by the union of the anterior subdivisions of the fifth and sixth cervical nerves, a particular paralysis results, due to inability to innervate certain muscles (the deltoid, biceps, brachialis internus, brachioradialis, sometimes the supinator brevis, sometimes the infraspinatus, and rarely also the subscapularis). These are the muscles that contract on stimulation of the so-called Erb's point, a spot two fingers' breadth behind the margin of the M. sternocleidomastoideus (See Electrodiagnosis). The arm cannot be lifted to the level of the shoulder, the forearm cannot be flexed at the elbow, nor can the upper arm be properly rotated lateralward. Sometimes the hand cannot be sufficiently supinated and the forearm and the hand are held in the pronation position.

This lesion is usually due to: (1) direct trauma at Erb's point; (2) compression between the clavicle and the first rib from forcible movements of the elevated arm backward and outward; or (3) tearing

of the nerve roots from the same cause (Clark, Prout, Taylor). Thus are explained the birth paralyses and the narcosis paralyses (postoperative or postanesthetic).

There is DeR in the paralyzed muscles. The periosteal-radial reflex is lost; the triceps reflex is retained; sensory disturbances are inconstant.

Fig. 565.—Diagram of the Plexus brachialis Showing the Location of the Lesion in Erb's Palsy. I = Truncus brachialis primarius superior; II = Truncus brachialis primarius medius; III = Truncus brachialis primarius inferior; $A_1$, $A_2$, $A_3$ = Anterior Branches; $P_1$, $P_2$, $P_3$ = Posterior Branches (Black); X = Truncus brachialis secundarius superior; Y = Truncus brachialis secundarius inferior; Z = Truncus brachialis secundarius posterior; L = Location of the Lesion in Erb's Palsy.

### (2) *Lower Lesion of the Brachial Plexus (Klumpke's Type)*

This lesion involves the part of the plexus arising from $C_8$ and $T_1$. It may depend on cervical rib, tumor, trauma, inflammation, etc.

There is atrophic paralysis of the small muscles of the hand (thenar, hypothenar and interosseous groups); oculopupillary symptoms (narrowing of lid-slit, enophthalmos, miosis); anesthesias in the domains of ulnar and median nerves; and, sometimes, partial paralysis of the flexors of the hand and fingers.

### (3) *Total Lesion of the Brachial Plexus*

When the whole plexus is involved in a lesion, all the muscles of the upper extremity are paralyzed. Occasionally a few nerve fibers may

escape, or a lesion that interrupts all fibers at first grows less later, giving rise to a somewhat irregular distribution of the disturbance of function of the various motor and sensory nerves arising from the plexus.

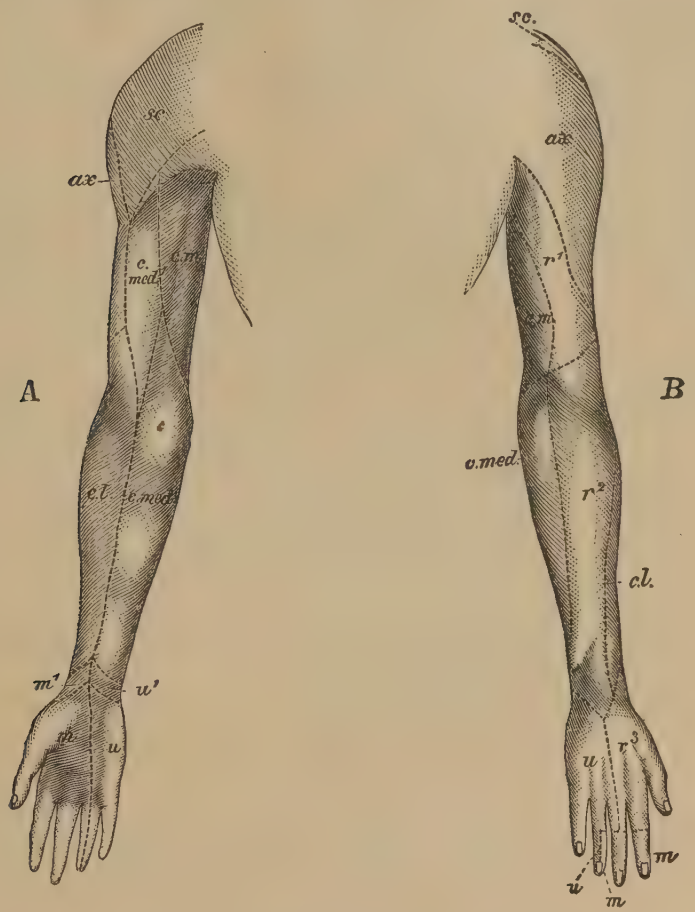


Fig. 566.—Areas Supplied by the Cutaneous Nerves of the Upper Extremity. (After A. Rauber, "Lehrb. d. Anatomie d. Menschen," published by G. Thieme, Leipzig.) A, Volar Surface; B, Dorsal Surface; *sc*, Nn. supraclaviculares; *ax*, N. axillaris; *cm*, N. cutaneus brachii medialis; *c. med*, N. cutaneus antibrachii medialis; *c. med*$^1$, Area of Upper Arm Supplied by Foregoing Nerve; *cl*, N. cutaneus antibrachii lateralis, a Branch of the N. musculocutaneus; $r^1$, N. cutaneus brachii posterior (Branch of N. radialis); $r^2$, N. cutaneus antibrachii dorsalis (Branch of N. radialis); $r^3$, Branch of N. radialis on the Back of the Hand; *u*, N. ulnaris (ramus dorsalis manus and ramus volaris manus) in the Hand; $u^1$, ramus cutaneus palmaris of N. ulnaris; *m*, N. medianus in the Hand; $m^4$, Its ramus palmaris.

These total lesions are rare; they are nearly always traumatic, seldom neuritic, in origin.

### (4) *Lesions of Single Peripheral Nerves, Branches of the Brachial Plexus*

These are sufficiently well shown in the tables on pages 357-58.

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## Motor and Sensory Phenomena Accompanying Lesions of Single Branches of the Plexus brachialis ($C_5$—$Th_2$)

| Nerve | Muscles Innervated | Movements Concerned in Paralysis or Spasm | Topography of Sensory Disturbance (Anesthesia, Neuralgia or Paresthesia) |
|---|---|---|---|
| *N. supra-scapularis.* | M. supraspinatus.<br>M. infraspinatus. | Lateral rotation of arm; holding head of humerus in joint cavity. | ..... |
| *Nn. subscap-ularis.* | M. subscapularis.<br>M. teres major and minor.<br>M. latissimus dorsi.<br>M. serratus poste-rior inferior. | Medial rotation, ab-duction and extension of upper arm. | ..... |
| *N. dorsalis scapulae.* | M. levator anguli scapulae.<br>M. rhomboideus.<br>M. serratus posticus. | These muscles hold the scapula down and bring it near the spine; when paralyzed, the scapula is dislocated up-ward and lateralward and its medial margin stands out from the thorax like a wing. | ..... |
| *N. thoracicus longus.* | M. serratus anticus major. | This fixes the scapula on elevation of the arm above the horizontal; in paralysis, this is no longer possible, and, at rest, there is winglike projection of lower part of scapula; on extend-ing arm forward, the whole scapula projects. | ..... |
| *Nn. thoracici anteriores.* | M. pectoralis major.<br>M. pectoralis minor. | Adduction of the arm. | ..... |
| *N. axillaris (circumflex).* | M deltoideus.<br>M. teres minor. | Elevation of the arm as far as the horizontal level by the deltoid. Function of the teres minor is lateral rota-tion of the arm. | Skin over posterior half of deltoid and back of upper part of upper arm. |
| *N. musculo-cutaneus.* | M. coracobrachialis.<br>M. biceps.<br>M. brachialis inter-nus. | Flexion of the fore-arm in positions other than that of supina-tion; in paralysis this is impossible, though flexion may occur in the supination position by means of the M. brachioradialis. | Radial half of the flexor surface of the forearm and a band along the radial side of the extensor surface. |

MOTOR AND SENSORY PHENOMENA ACCOMPANYING LESIONS OF SINGLE BRANCHES OF THE PLEXUS BRACHIALIS ($C_5$ — $Th_2$)—Continued

| Nerve | Muscles Innervated | Movements Concerned in Paralysis or Spasm | Topography of Sensory Disturbance (Anesthesia, Neuralgia or Paresthesia) |
|---|---|---|---|
| ***N. cutaneus brachii medialis*** (purely sensory). | ..... | ..... | Skin on the anterior, medial and posterior surfaces of the upper arm. |
| ***N. cutaneus brachii medius*** (purely sensory). | ..... | ..... | Ulnar half of the flexor and extensor surfaces of the forearm. |
| ***N. radialis.*** | 1. M. triceps.<br>M. supinator.<br>M. brachioradialis. | 1. Extension and supination of forearm; in paralysis, forearm can neither be extended nor supinated, and flexion in the semi-prone position is enfeebled. | 1. Back of the hand as far as the middle, backs of first three fingers, except of the terminal or of the middle and terminal phalanges. Dorsal surface of the thumb and lateral domain of the thenar eminence. |
| | 2. M. extensor carpi radialis and ulnaris. | 2. Dorsal flexion, adduction, and abduction of the hand. | 2. Skin of the dorsal surface of the forearm. |
| | 3. M. extensor digiti communis.<br>M. pollicis longus and brevis.<br>M. abductor pollicis longus. | 3. Extension of the proximal phalanges of the fingers, extension and abduction of the thumb. | 3. Skin of the lateral surface of the upper arm. |
| ***N. medianus.*** | 1. M. pronator quadratus. | 1. Pronation of the forearm. | Palm of the hand as far as the fourth metacarpal bone; volar surface of the first three and radial side of the fourth digit. |
| | 2. M. palmaris longus.<br>M. flexor carpi radialis. | 2. Flexion of the hand. | |
| | 3. M. flexor digitorum sublimis.<br>M. flexor digitorum profundus (radial half).<br>M. lumbricales I and II. | 3. Flexion of the middle phalanges, as well as flexion of the terminal phalanges of the middle and index fingers. | Dorsal surface of the second and third phalanges of thumb, index and middle finger. |
| | 4. All the muscles of the thumb except the M. adductor. | 4. Flexion and opposition of the thumb. | |
| ***N. ulnaris.*** | 1. M. flexor carpi ulnaris.<br>M. flexor digitorum profundus (ulnar half). | 1. Flexion of the hand (partly). | Palm of the hand corresponding to the fifth and the middle of the fourth metacarpal bones; volar surface of the little finger and ulnar margin of the ring finger. The back of the hand as far as its middle; dorsal surface of the little finger, ring finger and the ulnar half of the middle finger, with the exception of the terminal phalanges. |
| | 2. M. interossei and lumbric. III and IV. | 2. Flexion of the proximal and extension of the terminal phalanges of the fingers; separation and approximation of the fingers. | |
| | 3. M. adductor pollicis. | 3. Adduction of the metacarpal bone of the thumb. | |

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## iii. Lesions of the Thoracic Nerves (Nn. thoracales)

The thoracic nerves send motor branches to the muscles of the back, the intercostal muscles and the abdominal muscles on each side (M. rectus, M. obliquus externus, M. obliquus internus [partly], and M. transversus [partly]). They send sensory fibers to the skin of the chest, abdomen and back. Lesions of the motor branches of the thoracic nerves seldom cause recognizable paralyses unless several nerves are simultaneously involved, since the muscles of the chest and back are innervated from several sources.

### (1) *Paralysis of the Muscles of the Back*

In *bilateral paralysis*, on sitting, the trunk "sinks together" in kyphosis; on standing, a lordotic position is assumed. The patient is unable, when bent forward, to straighten up without the help of the arms resting upon the thighs. *Unilateral paralysis* causes lateral curvature (scoliosis), with convexity toward the paralyzed side.

### (2) *Paralysis of the Abdominal Muscles*

In *unilateral paralysis*, the navel is dislocated toward the healthy side, a deviation that is increased on coughing or straining. On forced expiration, there may be bulging of the paralyzed side, and, on palpation, one can easily distinguish the relaxed paralyzed muscle from the tense contracted muscle of the healthy side.

In *bilateral paralysis*, there is lordosis of the lumbar spine, the pelvis being inclined strongly forward so that a plumb-line suspended from the thoracic vertebrae will fall against the middle of the sacrum. There is

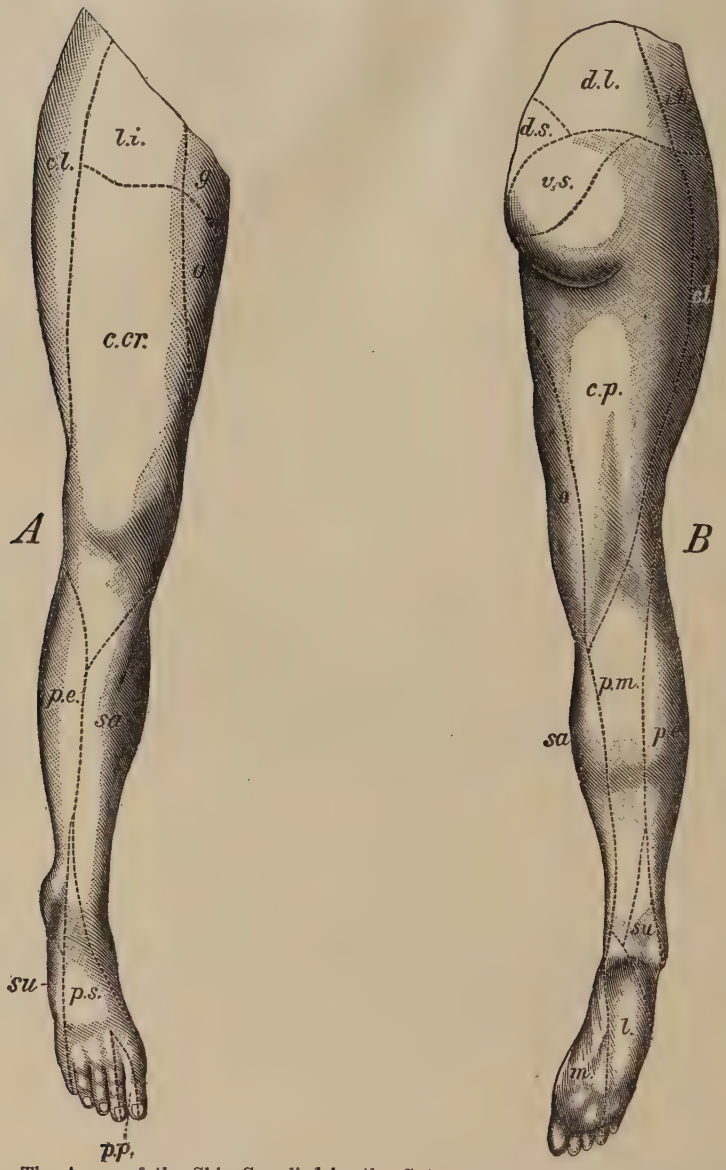


Fig. 567.—The Areas of the Skin Supplied by the Cutaneous Nerves of the Lower Extremity. A, Ventral Surface; B, Dorsal Surface. (After A. Rauber, "Lehrb. d. Anatomie d. Menschen," published by G. Thieme, Leipzig.) In B the Domain for the Dorsal Branches of the Plexus lumbosacralis Is Outlined on the Posterior Surface of the Hip, the Branches *d.l.* Being Dorsal Branches of the Nn lumbales (Nn clunium superiores); *d.s.*, Dorsal Branches of the Nn sacrales (Nn clunium inferiores); *v.s.*, Area Supplied by the N. perforans lig. tuberososacrum; *i.h.*, N. iliohypogastricus; *g*, Area of Distribution of the N. ilioinguinalis and N. spermaticus externus; *l.i.*, N. lumbo-inguinalis; *c.l.*, N. cutaneus femoris lateralis; *c.cr*, rami cutanei anteriores of N. femoralis; *o*, N. obturatorius; *c.p.*, N. cutaneus femoris posterior; *sa*, N. saphenus; *p.l.*, lateral, *p.m*, Posterior Branch of N. peroneus to the Leg; *su*, N. suralis; *p.s.*, N. peroneus superficialis (N. cutaneus dorsalis medialis et N. cutaneus dorsalis intermedius et Nn. digitales dorsales pedis); *p.p.*, N. peroneus profundus (Nn. digitales dorsales hallucis lateralis et digiti secundi medialis); *m*, N. plantaris medialis; *l*, N. plantaris lateralis.

marked projection of the abdomen in front and of the nates behind. Lying on his back, the patient cannot rise except through the aid of his arms. Forced expiration (in singing, coughing, crying) is no longer possible; there may be difficulty in defecation and micturition owing to interference with the prelum abdominis. For the distribution of anesthesias, neuralgias and paresthesias in the domain of the thoracic nerves (or intercostal nerves), see atlases. Unilateral or bilateral loss of the various abdominal reflexes may be helpful in localizing diagnosis (see reflexes).

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### iv. Lesions of the Lumbar, Sacral and Coccygeal Nerves

Lesions of the lumbar and sacral plexuses, and of the nerves derived from these plexuses, are far less common than lesions of the plexuses and nerves supplying the upper extremities.

The posterior branches of the lumbar nerves supply the short and long muscles of the back in the lumbar region (M. erector trunci and M. quadratus lumborum), and send sensory branches to the skin of the lumbar region (close to the spine) and of the upper part of the buttock. The anterior branches of the three upper lumbar nerves and a part of the fourth nerve form the plexus lumbalis, while part of the fourth together with the fifth lumbar nerve helps to form the plexus sacralis.

The sacral nerves (and N. coccygeus) supply, with their posterior branches, the skin over the sacrum and the adjacent part of the buttock; the anterior branches help to form the sacral plexus and the pudendal plexus.

The nerve roots forming these plexuses, the plexuses themselves, or the peripheral nerves distal from the plexuses, may become involved in tumors arising in the spine, the bones, the organs of the pelvis, the retroperitoneal glands, or the femur; or they may be injured by psoas abscesses, or in various forms of neuritis (gouty, alcoholic, diabetic).

The distribution of the sensory disturbances accompanying lesions of these nerves are well shown in the illustrations. The motor and sensory disturbances can be easily gathered from consultation of the following tables.

# 1. Branches of the Plexus lumbalis

| Nerves | Muscles | Movements | Sensation |
|---|---|---|---|
| ***N. iliohypogastricus.*** | Lower part of abdominal muscles. (M. obliquus internus and M. transversus abdominis). | ..... | Skin over the M. gluteus medius, and over lowermost part of abdomen. |
| ***N. ilio-inguinalis*** (purely sensory). | ..... | ..... | Skin of the groin and of the external genitals. |
| ***N. genitofemoralis.*** (*a*) ***N. lumbo-inguinalis.*** | ..... | ..... | Skin of the subinguinal region. |
| (*b*) ***N. spermaticus externus.*** | M. cremaster. | Retraction of the testicle. | Anterior part of skin of scrotum and adjoining thigh. |
| ***N. cutaneus femoris lateralis*** (purely sensory). | ..... | ..... | Skin of lateral surface of thigh. |
| ***N. obturatorius.*** | M. gracilis.<br>M. adductor brevis.<br>M. adductor longus.<br>M. adductor magnus.<br>M. obturator externus. | Adduction of the thigh; crossing of the legs. Lateral rotation (only in part), and this less important than the rotary function of the sciatic nerve. | Skin of the medial surface of the lower half of the thigh. |
| ***N. femoralis.*** | M. iliopsoas.<br>M. sartorius.<br>M. pectineus.<br>M. quadriceps femoris. | 1. Flexion of the thigh. 2. Raising the trunk in the recumbent position without use of the hands. 3. Extension of the leg. Walking and standing. | Skin of the anterior surface of the thigh and of the medial surface of the leg and foot (medial malleolus, medial margin of the foot as far as the great toe). |

# 2. Branches of the Plexus sacralis

| Nerves | Muscles | Movements | Sensation |
|---|---|---|---|
| ***N. gluteus superior*** (purely motor). | 1. Mm. gluteus medius and minimus.<br>2. M. pyriformis<br>3. M. tensor fasciæ latæ. | 1. Medial rotation and abduction of the thigh (paralysis causes waddling gait).<br>2. Lateral rotation of thigh.<br>3. Flexion of thigh. | ..... |

1. Branches of the Plexus sacralis—Continued

| Nerves | Muscles | Movements | Sensation |
|---|---|---|---|
| ***N. gluteus inferior*** (purely motor). | M. gluteus maximus. | Extension of the thigh at the hip; on fixation of the lower extremity, it extends and inclines the trunk. Paralysis makes standing upright when the trunk is inclined forward impossible without the use of the arms; also causes inability to mount steps, jump or rise from a chair. Attempt to stand on a chair dislocates the pelvis markedly forward. | ..... |
| ***N. cutaneus femoris posterior*** (purely sensory). | ..... | ..... | Lower part of skin of buttock and posterior surface of thigh. |
| ***N. ischiadicus (sciatic nerve).*** | In the thigh: | | |
| | 1. M. gemelli. M. obturator internus. M quadratus femoris. | Lateral rotation of the thigh. | |
| | 2. M. biceps femor. M. semitendinosus. M. semimembranosus. | Flexion of the leg. | |
| ***Branches of the sciatic:*** | | | |
| ***(1) N. peroneus.*** | | | |
| ***(a) superficialis.*** | Mm. peroneus longus and brevis. | Dorsal flexion and pronation of foot. | Skin of lateral and of posterior surface of leg and of dorsal surface of foot. |
| | M. tibialis anterior. | Dorsal flexion and supination of foot. | |
| ***(b) profundus.*** | Mm. extensor digiti, longus and brevis. | Extension of toes. | |
| | Mm. extensor hallucis, longus and brevis. | Extension of great toe. | |
| ***(2) N. tibialis.*** | M. gastrocnemius. M. soleus. M. plantaris. | 1. Plantar flexion of the foot, and adduction. | Skin of the heel and sole of the foot and of the lateral margin of the foot. |
| | M. tibialis posterior. Mm. flexor digiti com. longus and brevis. | 2. Flexion of the toes. | |
| | M. flexor hallucis longus. Mm. interossei, abductor and adductor hallucis. M. abductor digiti minimi. | | |

## 3. Branches of the Plexus pudendus and Plexus coccygeus

| Nerves | Muscles | Movements | Sensation |
|---|---|---|---|
| *Nn.hemorrhoidalis inferior and medius.* | Mm. sphincter ani externus and internus. M. levator ani; Vesica urinaria (M. detrusor and M. sphincter vesicæ). | Continence of the bladder and rectum. | ..... |
| *N. pudendus.* | M. transversi perinei. M. bulbo- and ischiocavernosus. M. sphincter ani externus. | Defecation; erection of penis; ejaculation of semen. | Skin of perineum, posterior part of scrotum (in the male) labia majora and minora (in the female). |
| *N. dorsalis penis.* | ..... | ..... | Skin and mucous membrane of the penis. |
| *Plexus coccygeus.* | M. sphincter ani externus and M. levator ani. | Rectal function. | Skin about the anus and over the coccyx. |

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### (b) *Diseases of the Cerebral Nerves (Nn. cerebrales)*

Under this heading we shall consider briefly the topical diagnosis of lesions involving the twelve "pairs" of cerebral nerves. Some of these nerves are purely sensory (*e. g.,* Nn. olfactorii; Nn. optici; Nn. acustici, etc.), some are purely motor (*e. g.,* Nn. oculomotorii), and some contain both motor and sensory fibers (*e. g.,* Nn. trigemini).

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#### i. N. I. The Olfactory Nerves (Nn. olfactorii)

Loss of smell (*anosmia*) may be due to interference with breathing from nasal obstruction (*anosmia respiratoria*), the olfactory stimuli thus being unable to reach the beginnings of the nerves of smell, as in hypertrophic rhinitis, polyp, etc. When it is the choanae that are thus obstructed, the loss of the smell of foods, such an important part of what is popularly called their "flavor," is known as *anosmia gustatoria.*

The olfactory area in the nose, with the nerve beginnings, may be injured or destroyed in local disease (*e. g.,* lues), or the Nn. olfactorii may be injured anywhere in their course from the nose to the olfactory bulbs (fracture of the skull, meningitic process, tumors, etc.).

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#### ii. N. II. The Optic Nerve (N. opticus)

The N. opticus is, in reality, anatomically a part of the central nervous system. Developmentally considered, it is only the bipolar cells of the

retina that are analogous to other peripheral sensory neurons. It is customary, however, to consider the optic nerves and the optic tracts as parts of the peripheral nervous system. When blindness exists or visual acuity is diminished, and when there is any limitation of the visual field (hemianopsia, scotoma) for ordinary light or for colors, the possibility of injury of the optic nerve, or of the optic tract, must be considered.

The ophthalmoscopic examination decides whether a visual disturbance is dependent upon an optic neuritis (neuritis optica; choked disk), or upon an atrophy (primary or secondary) of the optic nerve.

**Optic neuritis** is common in lues cerebri, in hemorrhagic pachymeningitis, in different forms of meningitis, in nephritis, in chlorosis and in chronic lead poisoning. It occurs also in acute febrile diseases (scarlet fever, typhoid, influenza, rheumatism), in acute anemia, in diseases of the orbit and nasal sinuses, in otogenic abscesses, and in multiple sclerosis.

**Atrophy of the optic nerve** may be *secondary* (arising from a preceding neuritis optica or choked disk) or primary and bilateral (*e. g.,* in tabes, or in dementia paralytica). The optic atrophy of multiple sclerosis is usually partial and begins as a *temporal pallor* of the disks.

**Retinitis** occurs in nephritis, tabes, leukemia, anemia, gout and sepsis, morely rarely in malaria, typhoid and pneumonia.

**Choked disk** when bilateral is most often due to brain tumor or to hydrocephalus; it may occasionally depend upon brain abscess, hematoma of the dura, sinus thrombosis or lues cerebri. Unilateral choked disk is most often met with in disease of the orbit or of one of the paranasal sinuses.

**Retrobulbar neuritis** may be met with in nicotine poisoning, alcoholism, tabes or multiple sclerosis.

When there is **amblyopia** without marked change in the disk or retina we consider the following: (a) when there is *concentric contraction of the visual fields,* neurasthenia or hysteria; (b) when there is *hemianopsia,* some cerebral disease (apoplexy, lues cerebri, brain abscess, encephalitis, hydrocephalus, tumors of the base of the brain); (c) when there is *central scotoma,* we think of retrobulbar neuritis optica. (See also The Sense of Sight and Its Anomalies, and, Lesions of the Visual Conduction Path.)

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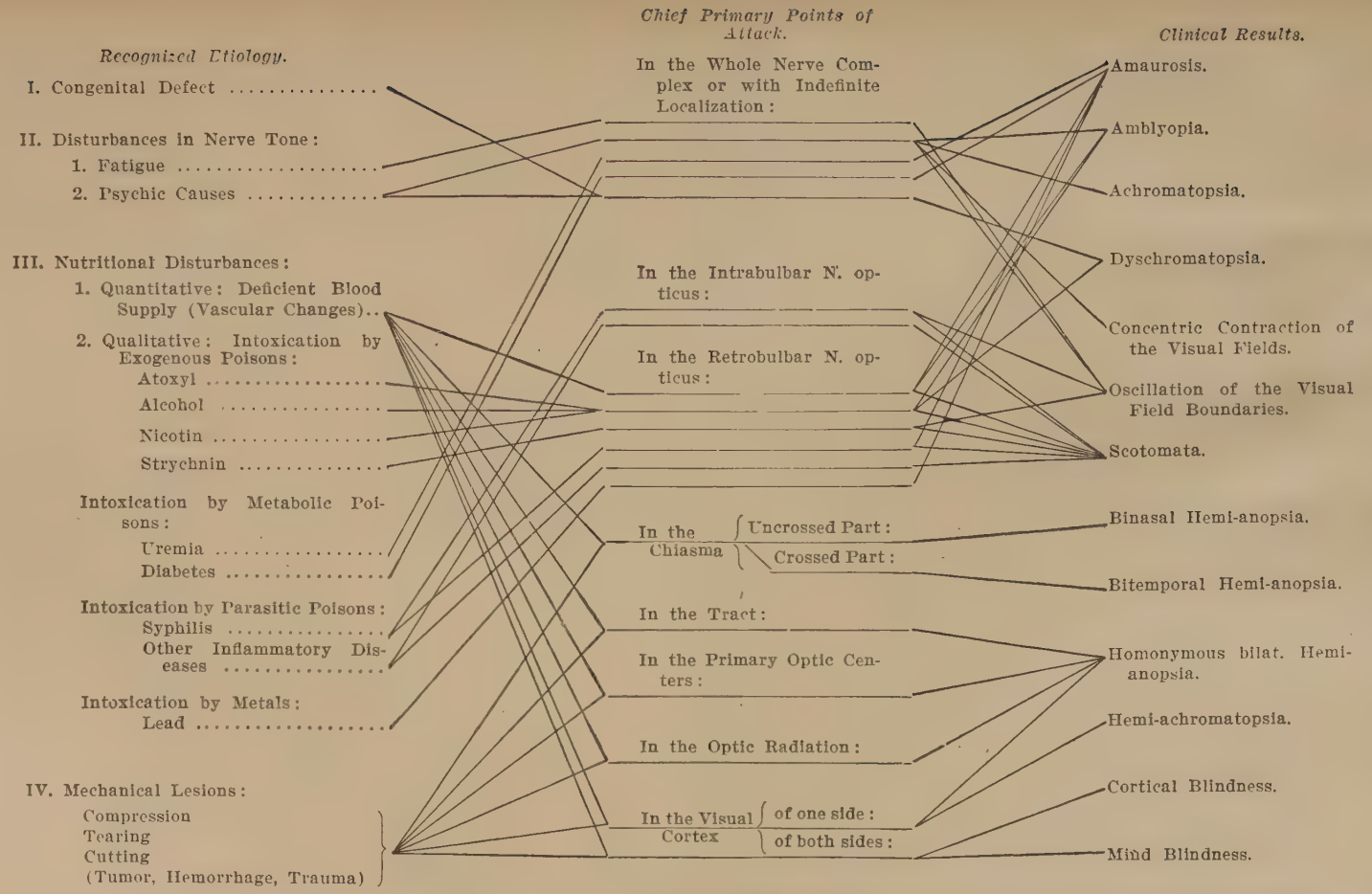


Fig. 568.—Survey of Disturbances in the Distribution of the N. opticus. (After O. Veraguth, "Die klin. Untersuch. Nervenkr.," published by J. F. Bergmann, Wiesbaden.)

### iii. N. III. The Oculomotor Nerve (N. oculomotorius)

This is a pure motor nerve. If all its fibers be interrupted, there will be **total paralysis** in its domain, including (1) ptosis, from inability to lift the upper lid by the M. levator palpebrae superioris, though it may still be a little lifted by contraction of the M. frontalis (innervated by the N. facialis); (2) the eyeball cannot be moved upward, downward, or medialward, or be rotated by the inferior oblique (paralysis of the Mm. rectus superior, inferior, medialis and obliquus inferior); (3) there will be loss of the power of accommodation; the pupil will be partly dilated, and will not react to light on direct illumination, on convergence, or on illumination of the eye of the opposite side (paralysis of autonomic fibers to M. ciliaris and to M. sphincter iridis).

In **partial oculomotor paralysis,** the branches to certain of the eye-muscles may escape. Occasionally the extrinsic muscles are paralyzed (*ophthalmoplegia externa*) while the intrinsic smooth muscles (M. sphincter iridis, M. ciliaris) retain their function. The latter, of course, are innervated by autonomic nerves running in the oculomotor nerve.

Oculomotor lesions are most common in basal meningitis (luetic) and in basal neoplasms, but may be met with in polyneuritis (*e. g.,* in diphtheria, typhoid, or influenza). The bilateral paralysis of the accommodation muscle (M. ciliaris), so common in diphtheria, is a paralysis in the domain of the autonomic nervous system.

It is sometimes difficult to distinguish an oculomotor paralysis due to lesion of the peripheral nerve from one due to involvement of the nuclei of origin of the nerve. Both are lower-motor-neuron paralyses. As a rule, in peripheral paralysis all the muscles supplied by the nerve are involved, while in nuclear affections single muscles are more likely to be picked out and the affection is more often bilateral than unilateral. Simultaneous involvement of both the intrinsic and extrinsic muscles of the eye points most often to peripheral lesion; separate involvement of intrinsic or extrinsic muscles points more often to nuclear lesion, though not always.

The diagnosis of a peripheral lesion is supported by the presence of other symptoms pointing to disease at the base of the brain.

The cases of periodic oculomotor paralysis are probably peripheral in origin, depending upon vasomotor changes that influence the blood supply of the peripheral nerve (anemia from vasoconstriction, compression from vasodilatation). See also, Examination of the Eye-muscle Movements (Strabismus, Diplopia).

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### iv. N. IV. The Trochlear Nerve (N. trochlearis)

This is a pure motor nerve, supplying only one muscle (M. obliquus superior). When injured, there is interference with movement of the eyeball downward and lateralward, with a slight squint medialward and upward. On looking downward, the patient sees two images, one above the other; the false image is below the true one, has its upper end tilted toward the other, and seems to the patient to be nearer to him than the true image. The double vision is especially noticeable on going down stairs; the steps appear double, and the patient usually feels a little giddy. There is slight strabismus convergens.

### v. N. V. The Trigeminal Nerve (N. trigeminus)

The *motor root* is small, and innervates the muscles of mastication. The *sensory root*, with its gasserian ganglion, is large. The sensory part of the nerve, peripheral to the ganglion, divides into three main branches, the motor fibers adjoining the third branch. These three divisions of the trigeminus are known as: (1) the ophthalmic nerve (ramus ophthalmicus), (2) the maxillary nerve (ramus maxillaris), and (3) the mandibular nerve (ramus mandibularis).

The *ramus ophthalmicus* (N. $V_1$) receives sensory impressions from the skin of the face and upper part of the head; also from the conjunctiva and cornea, the mucous membrane of the paranasal sinuses and of a part of the nose; in this branch run the secretory (autonomic) fibers for the lacrimal gland.

The *ramus maxillaris* (N. $V_2$), also purely sensory, innervates a part of the skin of the face, the mucous membrane of the upper part of the mouth and of the nasolacrimal duct; a part of the nasal mucous membrane and of the palate, as far as the arcus palatopharyngeus; and that of the sinus maxillaris (antrum of Highmore); it also carries the sensory fibers from the teeth of the upper jaw, and in its lingual branch run the taste fibers (belonging to the N. intermedius) for the anterior two-thirds of the tongue.

The *ramus mandibularis* (N. $V_3$) is (a) partly *motor*, supplying the muscles of mastication (M. masseter; M. temporalis; Mm. pterygoidei), the M. tensor tympani, the M. tensor veli palatini, the M. mylohyoideus and the anterior belly of the

M. digastricus, and (b) partly *sensory*, supplying the skin over the lower jaw, the external ear, and the temple; the mucous membrane of the tongue, cheek, and lower lip; and the lower teeth.

The most common primary peripheral disease of the N. trigeminus is that causing neuralgia (**tic douloureux**) of one or all of its branches, but

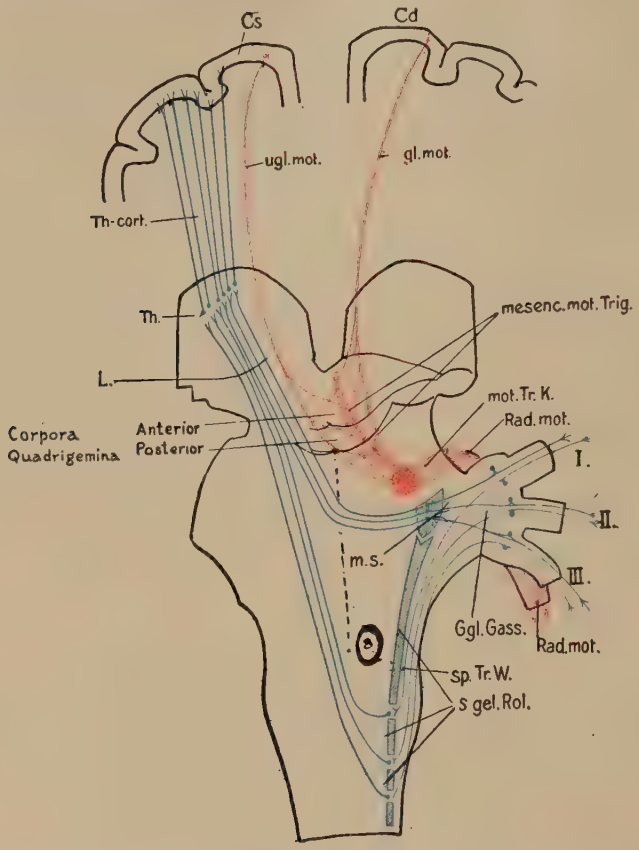


Fig. 569.—Intracentral Paths of the Trigeminus. Cs = Left Cortex; Cd = Right Cortex; Th. cort. = Thalmocortical Paths of N. V. Th = Relay Center for Sensory Fibers of N. V. in Thalamus; L = Lemniscus; Nucleus of V in Locus ceruleus; Rad. Mot. = Motor Root; Ggl. Gass. = Gasserian Ganglion; I, II, III = Divisions of V; S. gel. Rol. = Substantia gelatinosa of Rolando. (After O. Veraguth, "Die klin. Untersuch. Nervenkranker," published by J. F. Bergmann, Wiesbaden.)

lesions causing anesthesias and paralyses may be due to basal processes (meningitis, fracture of the base of the skull, caries, tumors). The healthy nerve may be affected in the neighborhood of the gasserian ganglion, or any one of the branches may be injured in its peripheral course.

**Total lesions** of the trigeminal nerve cause (1) anesthesia in the domains mentioned, (2) paralysis of the muscles of mastication, and (3)

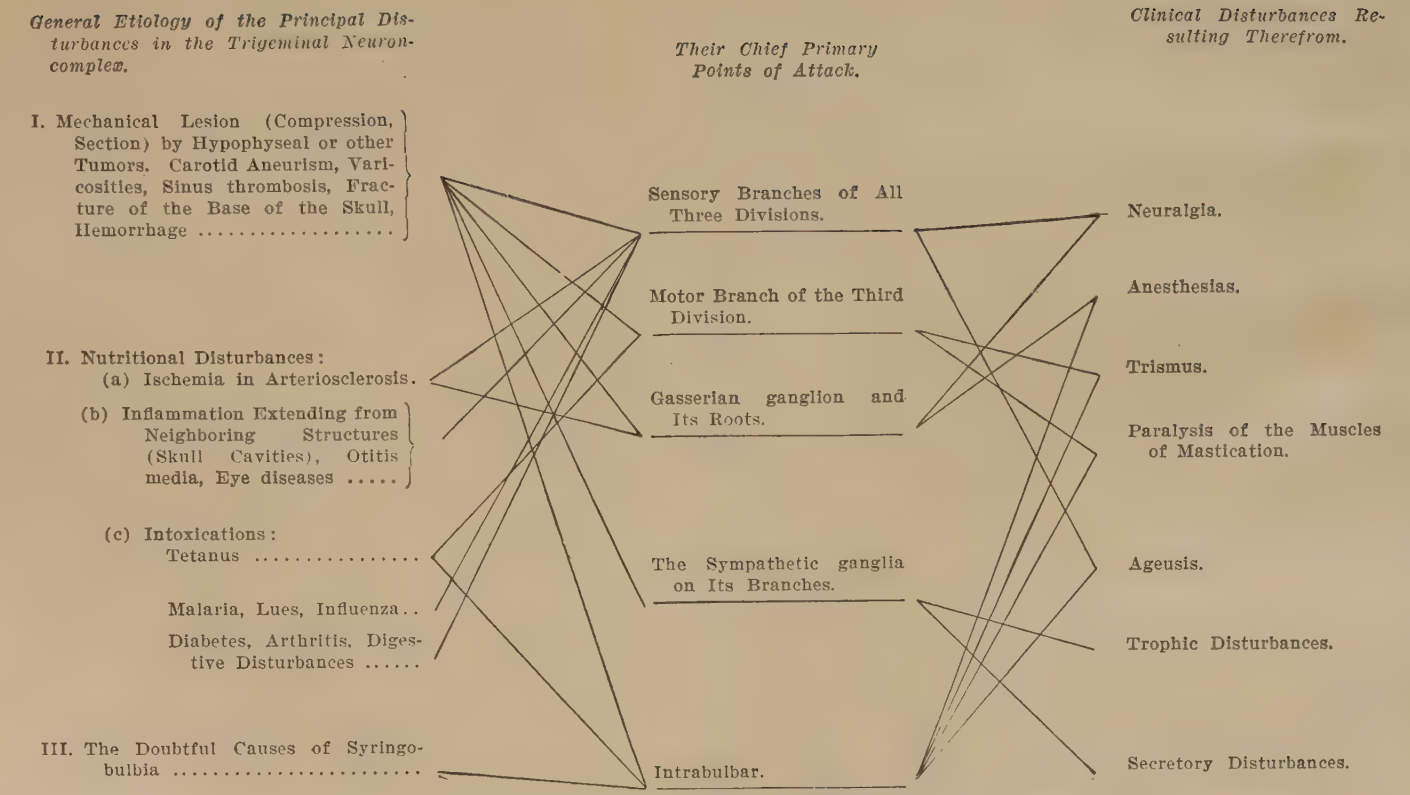
General Etiology of the Principal Disturbances in the Trigeminal Neuron-complex.
Their Chief Primary Points of Attack.
Clinical Disturbances Resulting Therefrom.
I. Mechanical Lesion (Compression, Section) by Hypophyseal or other Tumors. Carotid Aneurism, Varicosities, Sinus thrombosis, Fracture of the Base of the Skull, Hemorrhage .....
II. Nutritional Disturbances:
(a) Ischemia in Arteriosclerosis.
(b) Inflammation Extending from Neighboring Structures (Skull Cavities), Otitis media, Eye diseases .....
(c) Intoxications:
Tetanus .....
Malaria, Lues, Influenza..
Diabetes, Arthritis, Digestive Disturbances .....
III. The Doubtful Causes of Syringobulbia .....
Sensory Branches of All Three Divisions.
Motor Branch of the Third Division.
Gasserian ganglion and Its Roots.
The Sympathetic ganglia on Its Branches.
Intrabulbar.
Neuralgia.
Anesthesias.
Trismus.
Paralysis of the Muscles of Mastication.
Ageusis.
Trophic Disturbances.
Secretory Disturbances.

Fig. 570.—Survey of the Disturbances in the Functional Distribution of the N. trigeminus. (After O. Veraguth, "Die klin. Untersuch. Nervenkr.," published by J. F. Bergmann, Wiesbaden.)

loss of the corneal reflex on the diseased side. In addition to these trigeminal phenomena proper, such lesions may injure non-trigeminal fibers carried in the trigeminal nerves (autonomic and gustatory); thus the secretion of tears, and the secretion of the glands of the nasal mucous membrane, may be lacking on the diseased side, and taste may be disturbed in the anterior two-thirds of the tongue on that side.

Bilateral paralysis of the muscles of mastication (*diplegia masticatoria*) causes jaw-drop; in bilateral paresis, the chewing movements are enfeebled (*dysmasesia*). Fatigue on chewing is often an early sign in myasthenia gravis.

In unilateral paralysis of the masticatory muscles (*monoplegia masticatoria*), the patients can chew on the non-paralyzed side only; this is easily made out on palpation of the M. masseter. The patient cannot shove his lower jaw over to the healthy side; and on opening his mouth, the mandible deviates toward the paralyzed side.

**Partial lesions** cause symptoms of sensory irritation (hyperesthesias, neuralgic pains), or localized anesthesias. In distinguishing peripheral trigeminal lesions from central lesions, it may be borne in mind, (1) that nuclear trigeminal lesions are always accompanied by other symptoms referable to the pons or medulla oblongata; (2) that unilateral cerebral lesions never cause paralysis of the muscles of deglutition; and (3) that trigeminal anesthesias of cerebral origin are probably, always, only a part of a hemi-anesthesia.

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### vi. N. VI. The Abducens Nerve (N. abducens)

This purely motor nerve innervates only one muscle (M. rectus lateralis), a muscle that moves the eyeball directly lateralward. In lesions of this nerve, the eyeball (and the center of the pupil) cannot be directed lateralward further than the middle line; the paralysis is very easy to recognize. After a time, contracture of the antagonistic M. rectus medialis causes a convergent squint (strabismus convergens). The diplopia, due to the paralysis, appears on looking toward the side of the lesion, not on looking toward the other side. The two images stand beside one another, the false image being on the same side of the true image as the muscle paralyzed; that is, in paralysis of the left lateral rectus, the false image is to the left. The images grow farther apart on looking toward the paralyzed side.

Abducens paralysis is not uncommon. It may be due to compression from tumors, not only those situated at the base of the skull, but also from tumors elsewhere in the brain; to meningitic processes (luetic, tuberculous, pyogenic); or to congenital, or acquired, hydrocephalus. Peripheral lesions of the nerve are distinguished from nuclear paralysis by the pontile symptoms that accompany the latter.

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## vii. N. VII. The Facial Nerve (N. facialis)

The facial nerve proper is a pure motor nerve, innervating all the muscles of the face and, in addition, the M. buccinator, M. stylohyoideus, M. platysma, and the posterior belly of the M. digastricus; a branch from the fallopian canal goes also to the M. stapedius. The facial nerve, besides these motor fibers, carries, throughout a part of its course, (1) centrifugal autonomic fibers for the lacrimal, salivary and sweat glands, and (2) centripetal gustatory fibers for the anterior two-thirds of the tongue; the latter, passing from the N. lingualis (N. $V_3$) into the chorda tympani, go centripetalward through the facial nerve as far as the geniculate ganglion of the N. intermedius. Their further course is disputed, it being generally assumed that they pass through the N. petrosus superficialis major, or minor, back to the N. trigeminus, or to the N. glossopharyngeus, and thence into the brain.

If this nerve be irritated, we see *facial spasm;* if it be interrupted in its continuity, we see *facial paralysis.*

**Bell's palsy** (total unilateral peripheral facial paralysis) is easy to recognize. The face, even at rest, is strikingly asymmetrical, and the asymmetry becomes very marked on attempts at facial movement. On the paralyzed side, the wrinkling of the forehead is absent, the eye stays wide open (often so wide that the mucous membrane of the lower lid is exposed); tears run down over the face, the eye cannot be voluntarily closed, the angle of the mouth is drawn to the healthy side, and the nasolabial fold on the paralyzed side is absent. On expiration, the cheek bulges on the paralyzed side (buccinator paralysis); and, on attempts at whistling, air escapes from the mouth on that side.

Fig. 571.—Woman Exhibiting Facial Hemispasm (Right-sided). Tonic Phase of the Attack. (After J. Zabinskie, "La Nouvelle Iconographie de la Salpêtrière," published by Masson et Cie, Paris.)

Disturbances of taste, of salivary secretion, of sweat secretion, of tear secretion, and of hearing, may or may not occur, according to the site of the lesion (*vide infra*). DeR is demonstrable in the paralyzed muscles.

Facial paralysis due to disease of the

nerve must be distinguished (1) from nuclear paralyses, and (2) from supranuclear or cerebral paralyses.

DeR is demonstrable in the paralyzed muscles in peripheral lesions and in nuclear lesions, but not in supranuclear lesions. In both peripheral and nuclear lesions it is usual to have all the muscles of the face paralyzed, while in supranuclear lesions the muscles supplied by the so-called upper-facial—that is, the muscles of the forehead and eyelid—are not paralyzed.

In nuclear lesions the paralysis is always associated with other pontile symptoms (*q. v.*). These are absent in peripheral lesions, except in the

Fig. 572.—Complete Right Facial Palsy, Complicating Herpes Zoster in the Geniculate Zone: Edema and Slight Lateral Dislocation of Right Auricle. (After J. R. Hunt, Arch. Int. Med.)

instances in which the facial nerve is injured just at the base of the brain, in which event the cochlear and vestibular nerves may be simultaneously involved and other general cerebral symptoms coexist (tumor of cerebellopontile angle).

**Exact Localization of a Lesion Involving the Peripheral Part of the Facial Nerve** (Fig. 573).—If the nerve be injured in the fallopian canal between 1 and 2 in the figure, that is below the point of entrance of the chorda tympani, there will be facial paralysis without ageusia; if the injury lies between 2 and 3 there will be, in addition to the facial paralysis, ageusia on the anterior two-thirds of the tongue, and the salivary

secretion will be abnormal. If, in addition, there be hyperemia, the lesion will lie between 3 and 4, while if, still further, there be disturbances of the secretion of tears, the lesion is probably situated at the level

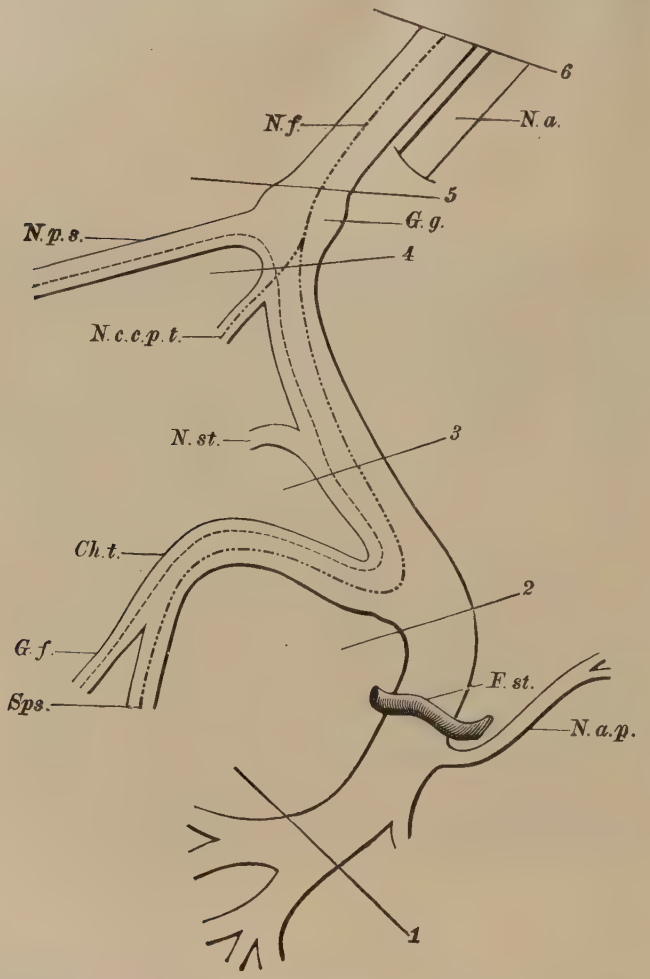


Fig. 573.—Diagram for Facial Paralysis Representing the Course of the Facial Trunk from the Base of the Skull to the Pes anserinus. *N.a.*, Auditory Nerve; *N.f.*, Facial Nerve; *N.p.s.*, Large Superficial Petrosal Nerve; *G.g.*, Geniculate Ganglion; *N.c.c.p.t.*, Communicating Branch to Tympanic Plexus; *N.st.*, Stapedius Nerve; *Ch.t.*, Chorda tympani; *G.f.*, Gustatory Fibers; *Sps.*, Secretory Nerve to Salivary Glands; *F.st.*, Stylomastoid Foramen; *N.a p.*, Posterior Auricular Nerve. (After W. Erb.)

of the geniculate ganglion between 4 and 5; when the lesion lies between 5 and 6, that is above the geniculate ganglion, there is no ageusia.

**Causes of Peripheral Lesions of Facial Nerve.**—Many cases of facial paralysis are due to exposure to cold ("rheumatic neuritis"); many depend upon extension of an inflammation from the middle ear; still others

are due to infectious processes, to fracture of the skull, or to caries of the temporal bone. Lesions of the nerve at the base of the brain are usually

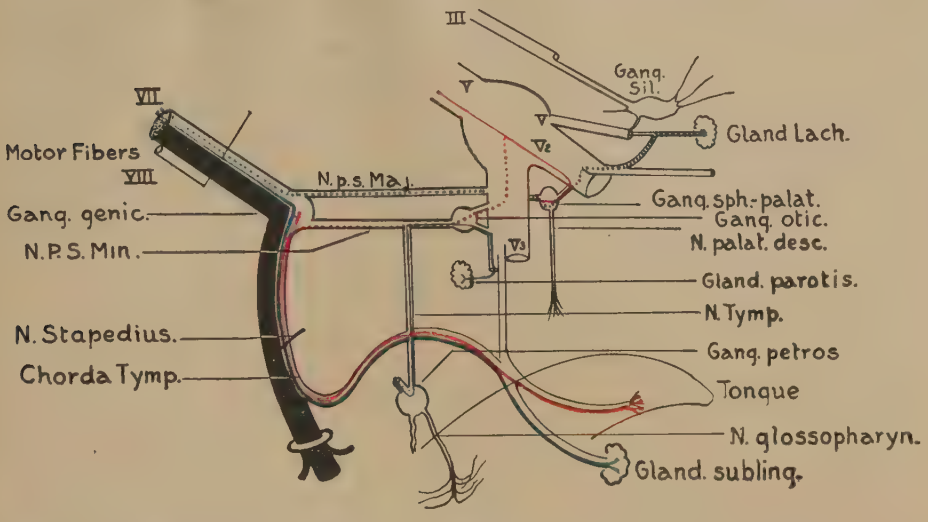


Fig. 574.—Schema of the Peripheral Connections of the Facial, Auditory, Trigeminal and Glossopharyngeal Nerves and the Sympathetic. (Modified from Veraguth.)

*Blue* = Fibers to Lacrimal and Salivary Glands; *Red* = Gustatory Fibers; *Black* = Motor Fibers of N. facialis; iii = N. oculomotorius; v = N. trigeminus with Its Three Branches, $v_1$, $v_2$, $v_3$; Gang. cil. = Ganglion ciliare; Gland. lach. = Glandula lacrimalis, the Bundles to This Gland Pass Out from $v_2$ in the Nervus zygomatico-temporalis, Passing Then by an Anastomosis to the N. lacrimalis from $v_2$; Gang. sph.-palat. = Ganglion sphenopalatinum; Gang. otic. = Ganglion oticum; N. palat. desc. = Nervus palatinus descendens; N. tymp. = Nervus tympanicus; Gang. petros. = Ganglion petrosum; N. glossopharyng. = Nervus glossopharyngeus; Chorda tymp. = Chorda tympani; N. p. s. min. = Nervus petrosus superficialis minor; N. p. s. maj. = Nervus petrosus superficialis major; Gang. genic. = Ganglion geniculi.

due to tumors (especially those of the cerebellopontile angle), or to meningeal inflammations (tuberculous, luetic).

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### viii. N. VIII. The Auditory Nerve (N. acusticus)

This nerve is made up of two parts, which have entirely different functions, the N. cochleae, or nerve of hearing proper, and the N. vestibuli, which has to do with equilibrium and with the setting of the eyes and of the head.

The peripheral lesions of the N. acusticus may be situated in the internal ear itself involving the membranous labyrinth (inflammations, hemorrhages, sclerotic processes), or they may be located in the nerve roots at the base of the brain (meningitis, tumor, caries). For the distinction between deafness due to middle ear disease and labyrinthine disease, see The Sense of Hearing and its Anomalies.

Circumscribed disease of the cochlea causes partial deafness; total destruction of the cochlea on one side causes complete unilateral deafness. In either case there may be subjective noises in the diseased ear; indeed subjective sensations may arise from irritation also in the cochlear paths or in the cortex. In labyrinthine disease, it is common to have certain parts of the tone-series more affected than others; the tones near the upper limit are most often involved; next in frequency, the tones near the lower limit; last of all, the tones at the middle of the series.

It is rare to find complete unilateral deafness from lesions of the cochlear paths above the superior olivary nucleus; since the paths a little above this undergo partial decussation, unilateral lesions higher up cause bilateral impairment of hearing, the impairment being greater in the hearing on the side opposite the lesion. Bilateral lesion of the auditory paths in the temporal lobes causes total bilateral deafness.

Since the N. cochleae and the N. vestibuli run close to one another from the labyrinth to the hindbrain, and since the cochlear and the vestibular paths diverge after the central nervous system has been entered, it is obvious that combined cochlear and vestibular symptoms point to peripheral injury, whereas lesions within the brain are more likely to injure one path without injuring the other.

If bilateral deafness (complete) occur before the fourth year of life,

the patient will never learn to speak (deaf-mutism); if it occur between the fourth and the seventh year, mutism does not always follow; if it occur after the seventh year, mutism rarely results.

Vestibular lesions, such as those accompanying Ménière's disease, are characterized by equilibratory disturbances (vertigo, nystagmus, disturbances of the Bárány reflexes). Among the signs of vestibular disturbance that should direct attention to its domain are: (1) nystagmus, (2) vertigo, (3) disturbances of orientation, of judgments regarding the position of the head, or of the body, in space, (4) loss of power to judge distances and directions, (5) sensations of sinking, or of being lifted, (6) inclined appearance of vertically placed objects, and (7) hypotony of the muscles.

Experimental nystagmus is interfered with in disease of the labyrinth and of the N. vestibuli, whereas it can be elicited, as in normal persons, in cerebellar disease provided the latter leaves the N. vestibuli uninjured.

In partial lesions of the labyrinth, or in irritation of the N. vestibuli, there is often spontaneous nystagmus; the caloric reaction may be diminished, but nystagmus appears on rotation of the body, and especially on sudden movements of the head (Bárány). For further details of the caloric reaction, and the "pointing error" tests, see the Vestibular Senses and Their Anomalies.

**Ménière's Disease.**—This is a form of vertigo occurring with disease of the internal ear (vestibular apparatus), usually due to hemorrhages into the labyrinth. The hemorrhage in turn may depend upon lues, gout, atherosclerosis, or one of the diseases associated with hemorrhagic diathesis.

The vertigo comes on in paroxysms. The patient often feels as though struck to the floor by a blow on the head. He may even be unconscious for a moment. He feels either that his body rotates, or that objects in the external world are rotating about him. It is important to learn the direction of these rotations (see Vestibular Syndromes). The paroxysms may be accompanied by nausea and vomiting, which may persist for several hours. There is usually labyrinthine deafness in the corresponding ear and often persistent tinnitus. Nystagmus and diplopia may be concomitant. The cases should be analyzed by Bárány's methods.

**Paralytic Vertigo.**—(*Gerlier's Disease*).—This is an endemic disease prevalent in certain parts of Switzerland. The patients complain of violent vertigo, diplopia, temporary amblyopia, difficulty in swallowing and chewing, and on examination show ptosis and paresis of the extremities and of the muscles of the neck. The paralysis is of the flaccid type. The disease is paroxysmal in character. In the intervals between the paroxysms the patients feel quite well. Each attack lasts a few minutes. The *kubisagara* of Japan, described by Miura, is probably the same disease. The nature of the disease is entirely unknown.

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### ix. N. IX. The Glossopharyngeal Nerve (N. glossopharyngeus)

This nerve is both sensory and motor. It carries (1) the taste fibers for the posterior third of the tongue and the soft palate; in addition it contains (2) the fibers of common sensibility from the middle ear, eustachian tube and part of the pharynx; (3) motor fibers to the M. stylopharyngeus and the M. constrictor pharyngeus; and (4) the autonomic secretory fibers to the parotid gland.

Loss of function of the nerve is characterized by (1) ageusia in the posterior third of the tongue and on the palate; (2) areflexia on stimulation of the pharyngeal mucous membrane; (3) anesthesia of the upper pharynx; (4) difficulty in deglutition; and (5) disturbances of parotid secretion.

Lesions of this nerve are practically always associated with lesions of adjacent cerebral nerves at the base of the brain (basal meningitis, neoplasms, gumma, or aneurism in the posterior fossa of the skull). Occasionally, pharyngeal disease (diphtheria, streptococcus angina) may paralyze the motor nerve endings in loco. Inflammations of the middle ear may start a neuritis of this nerve and lead to ageusia, or to increased salivary secretion.

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### x. N. X. The Vagus Nerve (N. vagus)

The N. vagus or pneumogastric nerve carries (A) cerebrospinal axons, and (B) autonomic axons.

(A) The **cerebrospinal axons** are partly (1) *motor,* innervating the striped muscles of the throat and soft palate, and, especially, the muscles of the larynx (the N. laryngeus inferior or N. recurrens, supplying all the laryngeal muscles except the M. cricothyroideus, which is supplied by the N. laryngeus superior), and partly (2) *sensory fibers,* (a) from the posterior circumference of the external auditory canal, (b) from the mucous membrane of the pharynx, from the lower margin of the velum palatinum downward, (c) from the epiglottis, larynx and respiratory passages, and (d) from the esophagus.

(B) The **autonomic fibers** include:

(a) *Centripetal fibers* from the respiratory organs, the digestive organs, and the heart and the aorta (including excitation-fibers for the respiratory center).

(b) *Centrifugal fibers* (preganglionic to the ganglia, and thence by postganglionic fibers to the viscera), including:

(ba) Fibers to the smooth muscle of viscera of the thorax and abdomen (respiratory; digestive; urogenital (?) ).

(bb) Inhibitory fibers for the heart.

(bc) Vasomotor fibers for the pulmonary and coronary arteries and for the arteries of the abdominal viscera.

(bd) Secretory fibers for the glands of the bronchi, esophagus, stomach, intestine, pancreas, kidney, and, perhaps, other abdominal organs.

### *Symptoms of Unilateral Vagus Lesions*

These include: (1) unilateral paralysis of the velum palatinum, the paralyzed half hanging a little lower on quiet breathing, and no movement being visible on the paralyzed side on phonation; (2) paralysis of the muscles of the throat, though this rarely causes marked disturbance of deglutition; (3) laryngeal paralysis, the vocal cord on the paralyzed side occupying the median position and not moving on phonation or on respiration; (4) occasionally, unilateral anesthesia of the pharynx and larynx.

### *Symptoms of Bilateral Vagus Lesions*

The symptoms mentioned above are present on both sides; the velum palatinum hangs low and shows no movement on phonation; the speech has a nasal twang; on attempting to drink, the fluid is returned through the nose (palatine musculature); deglutition is disturbed, especially for solid foods (pharyngeal musculature); there is inspiratory dyspnea, aphonia, and inability to cough (laryngeal musculature). In addition, autonomic disturbances are met with (tachycardia, alteration in the frequency and regularity of respiration, gastric disturbances).

### *Lesions of the Inferior Laryngeal Nerve (Recurrens Paralysis)*

The laryngeal muscles are divisible into two functional groups: (1) the closers of the glottis or adductors of the vocal cords (M. crico-aryte-

noideus lateralis, Mm. arytenoideus transversus, Mm. cricothyroideus externus and internus); and (2) the openers of the glottis, or abductors of the vocal cord (M. crico-arytenoideus posticus). According to Risien Russell, a special, separate bundle in the N. recurrens innervates the openers of the glottis. (See also Examination of the Larynx.)

In partial lesions of the N. recurrens, as a rule, the abductor muscle suffers first (Rosenbach-Semon law).

In unilateral lesions, the vocal cord, on the paralyzed side, occupies a middle position between adduction and abduction, the so-called cadaveric position. On phonation, it comes no nearer to the middle line; the vocal cord of the healthy side, however, goes beyond the middle line, and the arytenoid cartilages overlap. The vocal cord on the paralyzed side stands still during inspiration, while the cord of the other side is abducted.

In bilateral lesions, both vocal cords assume the cadaveric position, and remain in it, both on phonation and on respiration. There is aphonia and marked inspiratory dyspnea (stridor).

### *Lesion of the Superior Laryngeal Nerve*

Occasionally this is involved alone, in which event the voice is hoarse and deep, from faulty approximation of the thyroid and cricoid cartilages, due to paralysis of the M. cricothyroideus; there is also anesthesia of the laryngeal mucous membrane.

### *Vagal Irritation, and Vagal or Vasovagal Attacks*

Vagus irritation may cause marked bradycardia, which disappears under a hypodermic of atropin. Gowers has described characteristic vagal, or vasovagal, attacks, with gastric, respiratory, and cardiac symptoms; in the attack, there is palpitation, the arms go to sleep, there are subjective feelings of cold, there is slowness and difficulty in thinking, and, sometimes, mental fatigue and feelings of unreality; some of the patients have tetanoid spasms of the extremities. The condition was placed by Gowers in the borderland of epilepsy; it is often seen in hysterics. Some patients seem continuously to manifest an excessive vagotony. (See Examination of Autonomic Neuron Systems.)

Vagus lesions may occur at the base of the skull (then usually associated with paralysis of other cerebral nerves), or in the course of the nerve in the neck.

**The intracranial vagus lesions** may be due to meningitis, neoplasms, gumma, aneurism or periostitis.

**Cervical lesions of the vagus** are usually due to trauma, or to compression from enlargements of the cervical lymph glands. Recurrens paralysis may be due to mediastinal tumor, struma, aortic aneurism,

pleural thickenings (tuberculosis), or, occasionally, to dilatation of the left atrium in mitral stenosis. A collective review of the causes of recurrens paralysis will be found in the article by Félix.

**Vagus neuritis** may occur in alcoholism, in poisoning from lead or arsenic, in diphtheria, and in various infections. The vagal symptoms of tabes and of multiple sclerosis have not yet been fully explained.

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### xi. N. XI. The Accessory Nerve (N. accessorius)

This nerve yields the motor supply for (1) the M. sternocleidomastoideus and (2) the M. trapezius. The cervical nerves also send a few fibers to these muscles, more, however, to the M. trapezius than to the M. sternocleidomastoideus; it is asserted by some, probably erroneously, that the cervical nerves mentioned contain only sensory fibers; others believe that they contain motor fibers for the acromial portion of the M. trapezius.

In **unilateral sternocleidomastoid paralysis,** the head inclines toward the healthy side, the chin is turned toward the paralyzed side and slightly elevated, the head and chin cannot be well rotated toward the healthy side, and efforts to make the rotation are not associated with normal tension and bulging in the paralyzed muscle. In bilateral paralysis of this muscle, the patient cannot, while lying down, press his chin against his chest.

In **unilateral accessorius lesion** with paralysis of the M. trapezius, the shoulder is lower than normal, is displaced forward, the clavicle being lower and somewhat rotated; the scapula is farther than normal from the midline, is higher than it should be, and its lower angle is dislocated

medialward, and is separated a little from the thoracic wall, though the whole scapula does not separate from the wall as in serratus palsy. The rotation of the scapula into the boat-position of Duchenne, depends especially on paralysis of the acromial part of the muscle and this sometimes escapes in pure accessorius lesions. The shoulder cannot be lifted (except by the M. levator anguli scapulae), and since the scapula cannot be rigidly fixed, the arm movements suffer, especially elevation of the arm from the side.

In **bilateral accessorius lesions,** both shoulders sink forward, the thorax looks narrowed, the back is arched from side to side, and the clavicles are more prominent than normal. On asking the patient (1) to draw the shoulders back (middle and lower parts of Mm. trapezii), and (2) to shrug the shoulders up (upper portions of muscles), one notices the absence of the contours of the contracting muscles, normally so striking.

Irritation of one N. accessorius may cause spastic torticollis, or so-called **accessory cramp,** but this spasm does not usually have the tendency to limit itself to a definite nerve domain; it usually begins in one muscle, and, in the course of the disease, involves others.

The accessory nerve may be injured alone, or in combination with adjacent cerebral nerves (N. vagus, N. hypoglossus). Caries of the cervical spine often injures this nerve on one, or both sides; or the nerve may be involved in a meningitic or neoplastic process near the foramen magnum. Surgeons sometimes injure the nerve in operations on the neck.

In long standing paralysis of the M. trapezius, the dislocation of the scapula can sometimes be overcome by fastening its medial margin to the spine with a piece of the fascia lata (Rothschild).

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## xii. N. XII. The Hypoglossal Nerve (N. hypoglossus)

This is the motor nerve of the tongue (supplying the M. genioglossus, M. styloglossus, as well as the intrinsic muscles of the tongue); it also innervates the geniohyoid, omohyoid, sternohyoid, hypothyroid and sternothyroid muscles. For testing the hypoglossal functions, see Movements of the Tongue.

In **unilateral lesions of the N. hypoglossus,** the tongue is not protruded straight, but deviates obliquely toward the paralyzed side; the raphé forms a curve, the concavity of which is directed also toward the paralyzed side. The tongue on the side paralyzed wastes away, looks thin, wrinkled and relaxed, and electrical DeR is present. There may be but little disturbance of speech (except difficulty with "sh" and "x"), deglutition or mastication. Sensation is normal. Fibrillation points to nuclear, rather than to peripheral, lesion.

**Bilateral atrophic paralyses** of the tongue (in which the tongue lies immobile in the mouth and can neither be protruded nor moved lateralwards, interfering much with (1) the transport of food within the mouth and (2) the pronunciation (of the linguals and dentals) are, apparently, never peripheral, but always nuclear, in origin; they are usually associated with lesions of other cerebral nerves.

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## 2. Diseases of the Autonomic Nerves

From what has been said in the sections dealing with the method of examining the functions of the centripetal and centrifugal autonomic neuron systems (mesencephalic, bulbar, sympathetic, sacral), it will be understood that it is comparatively easy to refer certain symptoms to definite parts of the autonomic system. It is by no means easy, however, as yet, to decide what symptoms in these various domains depend upon lesions in the peripheral autonomic neurons proper, and what depend upon the higher sets of neurons superimposed upon them, since all the autonomic and sympathetic reflexes are subordinate (1) to higher reflex centers in the spinal cord, and (2) also, especially, to cerebral activities. The main facts regarding the significance of disturbances of the pupillary reflexes, and of the genito-urinary and rectal reflexes, are described elsewhere. Here attention must still be called to (1) lesions of the cervical sympathetic, (2) certain visceral neuralgias and (3) sympathicotonia and vagotonia.

### (*a*) *Lesions of the Cervical Sympathetic*

These may be irritative, or destructive.

*Irritation of the cervical sympathetic* is characterized by dilatation of the pupil, flattening of the cheek, widening of the lid slit, exophthalmos, symptoms of hyperidrosis, sluggish reaction of the dilated pupil, and neuralgic pains along the blood vessels, at the angles of the jaw, and in the ears.

Destructive lesions causing *paralysis of the cervical sympathetic* are characterized by the so-called Horner's symptom-complex: (1) contraction of the pupil on the same side (miosis), with retention of reaction to light, though the light reaction

may be sluggish and incomplete; (2) narrowing of the lid slit (sympathetic ptosis), due to loss of tonus in the smooth muscle of the upper lid, the pupil not being covered; the capacity to lift the lid without contraction of the M. epicranius is retained; (3) retraction of the eye (enophthalmos), due to paralysis of the M. orbitalis, and to atrophy of the fat in the orbit; (4) sometimes, dilatation of the blood vessels on the same side of the face and head; (5) anidrosis of the same side of the face; and (6) emaciation of the same side of the face.

Sympathetic ptosis is easy to differentiate from ptosis due to oculomotor paralysis. It should be borne in mind, however, that sympathetic ptosis may depend, not upon lesion in the cervical sympathetic, or upon a lesion of the centrum ciliospinale in the spinal cord, but upon injury to the ventral roots of the first or second thoracic nerves ($T_1$, $T_2$).

### (*b*) *Visceral Neuralgias*

Violent neuralgic pains are sometimes felt in the internal organs when they are diseased, or when the nervous system is diseased (*e. g.*, gastric crises, gastralgia, enteralgia, hepatalgia, nephralgia, etc.). The pains of renal colic, pancreatic colic, hepatic colic, dysmenorrhea, etc., should also be mentioned. The explanation of these pains is not yet clear. Some of them are apparently associated with smooth-muscle-spasm.

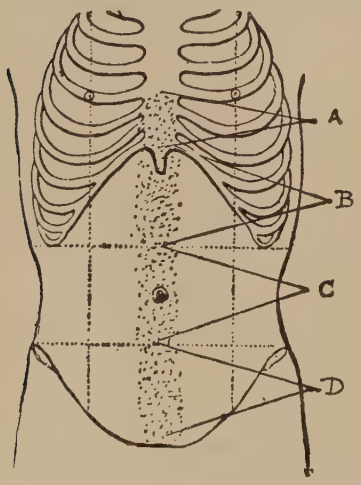


Fig. 575.—The Shaded Parts Show the Areas in Which Pain Is Felt in Affections of the Digestive Tube. A, Area in Affections of the Esophagus; B, Area in Affections of the Stomach; C, Area in Affections of the Small Intestine; D, Area in Affections of the Large Intestine. (After J. Mackenzie, "Symptoms and Their Interpretation," published by Shaw & Sons, London.)

The segmental pains, or hyperesthesias in the skin (*Head's zones* of referred pain) due to visceral disease, find their explanation, in my opinion, in abnormal irritation of the centripetally conducting sympathetic neurons, which, terminating upon the ganglion cells in the spinal ganglia, so irritate the peripheral cerebro-spinal sensory neurons as to give rise to sensations referred to the source whence these neurons normally gather impressions, that is the skin.

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### (*c*) *Vagotonia and Sympathicotonia*

These conditions are described elsewhere (See Examination of Autonomic Neuron Systems).

## C. Diagnosis of Lesions of the Spinal Cord

(*Medulla spinalis*)

In localizing lesions of the spinal cord we pay attention especially to two points: (1) the segmental level or levels involved, and (2) the amount of white matter and gray matter involved in the transverse direction at each level affected.

For the localization of disease in the spinal cord it is essential to think of it as made up of single segments, these segments in turn being united manifoldly with one another, and, by means of long afferent and efferent paths, with the higher parts of the nervous system (cerebrum, medulla and pons, cerebellum).

This view is in accord with the original metameric structure of the body of vertebrate animals. For each metamere, or segment, there is a nervous part (neurotome), a muscular part (myotome), a cutaneous part (dermatome), a general mesoblastic part (sclerotome), and probably a vascular part (angiotome). Often the viscera may be divided into portions (viscerotomes) corresponding to their innervation, since a neurotome may have a definite visceral connection through the autonomic nervous system.

A single neurotome gives rise, in bilateral arrangement, to (1) an afferent neuron system (sensory nerve; posterior root ganglion; posterior root; intramedullary continuation of posterior root fibers); (2) the motor, efferent, or centripetal, neuron system (anterior horn cells and dendrites; anterior roots; motor spinal nerve); (3) an autonomic system (centripetal and centrifugal) including both preganglionic and postganglionic fibers in both instances; and (4) certain associative neuron systems (including (a) intercalated cells, the functions of which are limited to the segment itself, and (b) associative neurons, with longer axons, which connect it with adjacent and more distant segments and with higher parts of the nervous system). The anterior and posterior roots of the spinal nerves, and the peripheral, sensory and motor nerves, lie outside of the spinal cord.

In development, the dermatome innervated by one posterior root, lies close to, and at right angles to, the spine, and extends from the middle line in the back to the middle line in front. This arrangement persists for the trunk throughout life, but in the extremities the dermatomes are pulled out into long, longitudinal

strips, which run the whole length of the limb. In embryonic life the dermatomes are sharply separable from one another, but, later on, they overlap to a certain extent, and there is also an overlapping, therefore, in the sensory innervation of the skin, the cutaneous area receiving nerve fibers not only directly from the posterior root chiefly supplying it, but also from the adjacent roots, above and below (C. S. Sherrington). This explains why experimental section of a single posterior root need not cause complete anesthesia. The overlapping appears to be more marked for the sense of touch than for the senses of temperature and pain, and for the hyperalgesia and herpes (Head's zones) that correspond to the autonomic metameric innervation.

This morphological arrangement explains why the anterior motor root of the spinal nerve does not innervate single muscles, but, instead, parts of different muscles (corresponding to the muscle-tissue derived from a single myotome). In development, the dermatome supplied by a given posterior root comes to be dislocated somewhat caudalward as regards the myotome innervated by the corresponding anterior, motor root (Sherrington); in lesions of a given segment of the spinal cord, therefore, the upper limit of the paralysis may lie somewhat higher in the body than that of the anesthesia due to the lesion.

In our analysis of the symptoms (motor, sensory, reflex, visceral) due to a disease of the spinal cord, we must try to answer the following questions: (1) Do the symptoms indicate that definite conduction paths of the spinal cord alone are implicated, the disease being limited to single or several neuron systems? or, (2) Has the spinal cord been injured more diffusely, over a smaller, or larger, part of its cross-section, owing to, say, a lesion that has paid no regard to single neuron systems or conduction paths? When the symptoms are due to clean-cut involvement of neuron systems (sensory, motor, or combined), we speak of simple or combined *system diseases* (*e. g.,* tabes; amyotrophic lateral sclerosis; ataxic paraplegia); when this is not the case we speak of *non-system diseases* (*e. g.,* complete and incomplete transverse lesions; hemilesions, and the like).

The latter may be due either to focal disease originating in the substance of the spinal cord itself (*e. g.,* myelitis, myelomalacia, tumor), or to pathological processes in the neighborhood of the spinal cord, extending, by contiguity, to it (*e. g.,* meningeal diseases, vertebral diseases).

The system diseases of the spinal cord may involve (1) the motor neurons, (2) the intramedullary continuations of the peripheral sensory neurons or so-called exogenous sensory fibers, or (3) the conduction paths in the cord, including (a) the spinopetal paths (pyramidal tract from the cerebral cortex, thalamospinal, rubrospinal, vestibulospinal, cerebellospinal, etc.), and (b) the spinofugal (including the upward relayed continuations of the afferent paths—the direct cerebellar tract, Gower's tract, etc.).

In every case, after we have decided upon the localization of the disease-process, we go on to a consideration of the special kind of pathological process underlying it. Our conclusions regarding the latter are

based usually upon the whole course of the disease and upon accompanying phenomena in other parts of the body (see Diagnosis of the Nature of the Lesion).

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## 1. Diagnosis of Involvement of Single and Multiple Neuron Systems in the Spinal Cord (System Diseases)

As examples, we may illustrate the localization of disease (a) in the upper motor neurons in the spinal cord, (b) in the lower motor neurons in the spinal cord, (c) in the upper and lower motor neurons simultaneously in the spinal cord, (d) in the peripheral sensory neurons in the spinal cord, and (e) in the peripheral sensory neurons and at the same time in other afferent and efferent neuron systems in the spinal cord (combined system diseases). For didactic reasons only the principal diagnostic points will here be referred to, free from bewildering detail. Once the main outlines have been thoroughly mastered, it is easy enough to fill in with finer matter.

### (a) *Lesions Involving only the Medullated Axons of the Upper Motor Neurons in the Spinal Cord*

(*Pyramidal-tract Lesions*)

Of the upper motor neurons it is only the more distal portions of their medullated axons (the uncrossed fibers in the anterior funiculus and the crossed fibers in the lateral funiculus) that are present in the spinal cord, since the cell-bodies of these upper motor neurons are located in the motor areas of the cerebral cortex and the proximal portions of their medullated axons lie in higher parts of the nervous system (centrum semiovale, internal capsule, pons, and medulla). (See Fig. 589, p. 438.)

Lesions of the axons of the upper motor neurons situated in the spinal cord cause paralysis, or paresis, of voluntary movement of the extremities, with hypertony (tendency to spastic contracture, increase of deep reflexes); there may be patellar clonus and ankle clonus; the Babinski phe-

nomenon is positive. The paralyzed muscles are not markedly atrophied; DeR is absent; sensation and the sphincters are normal (see Spastic Spinal Paralysis).

### (*b*) *Lesions Involving only the Lower Motor Neurons in the Spinal Cord*

(*Anterior-horn Lesions*)

When the lower motor neurons in the spinal cord are involved in a lesion, flaccid atrophic paralysis, with DeR on electrical examination, appears in the muscles innervated by the neurons affected. Thus, if the anterior horns in the cervical region are involved, the atrophic paralysis will affect the muscles of the hands, forearms, or arms, whereas if the localization be in the lumbar enlargement, the paralysis and atrophy will appear in the muscles of the lower extremities.

If the cell-bodies of the lower motor neuron concerned in a reflex arc be diseased there will be loss of the corresponding reflex. An especially important manifestation, pointing to the involvement of the lower motor neurons in the spinal cord rather than of the axons of the same neurons in the peripheral nerves, is the appearance of fibrillary twitching in the degenerating muscles.

If the disease be limited to the anterior horns and to the cell-bodies and dendrites of the lower motor neurons they contain, there is no disturbance of sensation or of the sphincter-functions (except in the instances in which the spinal sphincter levels $S_3$—$S_5$ are injured). Examples of such disease involving the lower motor neurons in the spinal cord are (1) acute and chronic anterior poliomyelitis and (2) the spinal form of progressive muscular atrophy.

### (*c*) *Combined Lesions of the Upper and Lower Motor Neurons in the Spinal Cord*

It is not uncommon to have the axons of the upper motor neurons in the spinal cord (pyramidal tracts) involved simultaneously with the lower motor neurons in the cord (anterior-horn cells), thus forming a systemic disease of the general motor conduction path in the cord. In such cases the atrophic flaccid paralysis with DeR and fibrillary twitching may be met with in the muscles of the upper extremities, while in the lower extremities there may be spastic paresis, with exaggeration of the deep reflexes. The sensibility and the sphincters are normal. Amyotrophic lateral sclerosis may be cited as an example.

### (*d*) *Lesions Involving only (or chiefly) the Peripheral Sensory Neurons in the Spinal Cord*

Under the influence of certain toxins, elective degenerations of the intramedullary continuation of the posterior roots of the spinal nerves (exogenous fibers) occur (*e. g.,* in tabes). The degeneration affects the posterior funiculi (Goll and Burdach) and the collaterals going into the grey matter, to the anterior-horn cells, to the cells of Clarke's column, etc. When the lesion is systemic and is limited to the sensory, centripetal neuron systems, the cutaneous sensibility and the deep sensibility (bones, joints, fascia, muscles) are disturbed. Sometimes there is anesthesia for all qualities of sensation; sometimes there is an elective loss of single modalities. In addition to the sensory disturbance, the reflexes, of which the degenerated neurons form the afferent limb of the arc, are lost. There is hypotony of the muscles associated with the bathyanesthesia, owing, probably, to the loss of the centripetal impulses concerned in the maintenance of the normal tonus. Though the power of the muscles is unaffected, there is incoördination of the muscles (ataxia), owing to the bathyanesthesia and hypotony. The function of the bladder is often disturbed owing to the loss of centripetal impulses from the bladder-wall consequent upon degeneration of the afferent neurons of the autonomic system. Symptoms of sensory irritation (lancinating pains) are common.

The principal criterion for distinguishing lesions of the radicular and intramedullary portions of the peripheral sensory neurons (*e. g.,* tabes) from extramedullary lesions of the peripheral sensory neurons is the topography of the sensory disturbance. In the radicular and in the intramedullary lesions, the anesthesias are radicular or segmental in distribution; in extramedullary lesions (*e. g.,* in neuritis), the anesthesias correspond in distribution to the domains supplied by peripheral nerves rather than to the domains supplied by posterior nerve-roots (spinal segments). Other criteria lie in the accompanying symptoms and in the etiology (see Special Diagnosis).

### (*e*) *Combined Lesions of the Peripheral Sensory Neurons (Posterior Funiculi) and of the Upper Motor Neurons (Pyramidal Tracts) within the Spinal Cord*

When the intramedullary continuations of the posterior roots and the pyramidal tracts of the lateral funiculi of the spinal cord are simultaneously involved in a systemic disease, the clinical phenomena that result are a combination of those met with in conditions *a* and *d* (above described); that is to say, the phenomena of spastic spinal paralysis are combined with the symptoms of tabes. Sometimes the sensory symptoms predominate, sometimes the spastic motor symptoms are the more promi-

nent. In the former case the tabetic syndrome is accompanied by a motor weakness of the extremities and by a positive Babinski or a positive Oppenheim sign. In the latter case, in addition to the syndrome of spastic spinal paralysis, certain tabetic symptoms appear (anesthesias, lightning pains, ataxia, vesical disturbances).

Examples of such combined motor and sensory systemic disease in the spinal cord will be found in the sections dealing with special diagnosis. (See ataxic paraplegia and Friedreich's ataxia.)

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## 2. Diagnosis of Lesions of the Spinal Cord not Limited to Specific Systems

*(Non-Systemic Diseases)*

We have next to consider the lesions that are not confined to specific neuron systems, but that, owing to their mode of origin, have a distribu-

tion regardless of the specific systems, involving sometimes more, sometimes less, of the different neuron systems present in the cord. Here belong: (a) the various transverse lesions, complete and incomplete, including the hemilesions; and (b) the multiple, focal, lesions of the cord.

### (*a*) *Transverse Lesions of the Spinal Cord*

Total or partial transverse lesions of the spinal cord may be due (a) to focal lesions in the substance of the cord itself (*e. g.*, transverse myelitis, hematomyelia, intramedullary tumors, gliosis, trauma), or (b) to extramedullary causes, leading to compression of the cord, including vertebral diseases (caries, fractures, tumors), and meningeal diseases (tumors, chronic inflammations). The origin and course of the disease, and the accompanying phenomena, permit one to decide as to their nature (see Special Diagnosis).

#### i. Total Transverse Lesions

When the spinal cord is completely interrupted we try to determine (1) the main division of the cord, whether cervical, thoracic, lumbar, or sacral, involved (gross level diagnosis); and (2) the precise segmental levels concerned (segmental level diagnosis). These level diagnoses will be taken up a little further on.

#### ii. Incomplete Transverse Lesions

These include (1) hemilesions of the cord (or Brown-Séquard's paralysis), and (2) incomplete transverse lesions other than hemilesions.

##### (1) *Hemilesions, or Unilateral Lesions, of the Spinal Cord (Brown-Séquard's Syndrome)*

Such lesions, due to trauma, gumma, myelitis, etc., give rise to a very characteristic clinical picture—the *Brown-Séquard syndrome.* On the side of the lesion there is (1) non-atrophic, spastic paralysis for muscles innervated by anterior horns caudal from the level of the lesion, with exaggeration of the reflexes and positive Babinski; (2) hyperesthesia for pain and temperature; (3) normal touch sensation; (4) loss of the deep sensibility (bathyanesthesia) and (5) incoördination of the voluntary movements (ataxia). On the heterolateral side of the body (opposite the lesion) there is (1) hypesthesia for touch; (2) anesthesia for thermal stimuli (thermanesthesia); and (3) loss of pain sense (analgesia).

Part of this clinical picture is easily explained by our knowledge of the conduction paths in the spinal cord, since the paths for deep sensibility run (uncrossed) in the homolateral posterior funiculus, while those for

the cutaneous sensations of temperature and pain run (crossed) in the lateral funiculus of the opposite side; the paths for touch run, chiefly crossed, through the white matter of the opposite side, but, partly uncrossed, through the white matter of the same side. The spastic paralysis is, of course, due to the involvement of the pyramidal tract. When the lesion is, as most often, in the thoracic part of the cord, the paralysis is a *hemiparaplegia;* if the lesion be in the cervical cord, paralyzing both the arm and the leg, it is a *hemiplegia spinalis.* The origin of the homolateral hyperesthesia is not easily explicable.

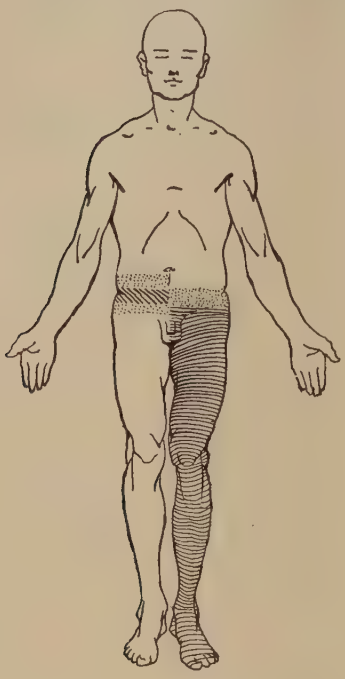


Fig. 576.—Brown-Séquard Syndrome. Right-sided Hemilesion of Spinal Cord.

In addition to the above phenomena, hemilesions are often accompanied by (1) vasomotor paralysis, with red, warm skin at first, later cyanosis and cold, on the side of the lesion, due to severance of the homolateral vasoconstrictor fibers of the lateral funiculus, and (2) a narrow, unilateral zone of anesthesia on the side of the lesion, at the level of the lesion, due in all probability to injury of the posterior root (peripheral sensory neurons) entering the spinal cord at this level.

Typical hemilesion is rare; more often the lesion takes in rather less than half the cord on one side, or, besides injury to one side, the lesion encroaches somewhat upon the other half also.

The symptomatology of Brown-Séquard's paralysis may be graphically represented in the following table:

| Conditions on the Side of the Lesion in the Spinal Cord (Homolateral) | Conditions on the Side Opposite the Lesion in the Spinal Cord (Heterolateral) |
|---|---|
| 1. Spastic motor paralysis.<br>2. Exaggerated reflexes.<br>3. Bathyanesthesia.<br>4. Hyperesthesia for temperature and pain.<br>5. Narrow segmental zone of anesthesia at level of lesion.<br>6. Vasomotor paralysis.<br>7. Sometimes ataxia. | 1. Analgesia.<br>2. Thermanesthesia.<br>3. Hypesthesia for touch.<br>4. Deep sensibility normal.<br>5. Normal mobility. |

### (2) *Incomplete Transverse Lesions Other Than Hemilesions*

Here the clinical picture will vary according to the portions of white or gray substance involved and the level at which they are involved.

Lesions involving chiefly the anterior horns of the gray matter will yield clinical pictures resembling anterior poliomyelitis. Lesions involving predominantly the posterior horns of the gray matter (*e. g.*, some cases of gliosis spinalis) will give rise to dissociated anesthesias (thermanesthesia and analgesia with retention of other forms of sensibility). Sometimes the anterior horns and posterior horns are simultaneously involved (see Gliosis and Syringomyelia).

## (*b*) *Multiple Focal Lesions of the Spinal Cord*

In certain diseases the spinal cord is simultaneously, or successively, affected at different levels by focal injuries. In such cases the cerebrum is often the site, also, of multiple lesions, and we have to do with the so-called "disseminated" or "scattered" cerebrospinal diseases (*e. g.*, sclerosis multiplex, myelo-encephalitis disseminata, lues cerebrospinalis).

The localizing diagnosis may be difficult, and even for some time impossible, since the symptoms may suggest, for a time, a single focal lesion, when in reality they are due to a number of lesions, which, taken together, have the same effect in interfering with the functions of neuron-systems as a single larger focus exerts; in other cases, small multiple foci of disease may be present in the spinal cord, which, by virtue of their position or of their small size, do not give rise to recognizable localizing symptoms. It is the cerebral phenomena accompanying the spinal phenomena that, as a rule, give us the clue to diagnosis; thus a beginning optic atrophy (temporal pallor), along with loss of abdominal reflexes, may, in a case of spastic paraplegia, lead us to the diagnosis of lesions disseminated through both brain and cord (multiple sclerosis).

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## 3. General Focal Localization or Gross Level-Diagnosis in the Spinal Cord

The table on the following page will be found helpful for a general, orienting, localization of the general level of lesions of the spinal cord.

## 4. Precise Level Diagnosis of Lesions in the Spinal Cord

(*Segmental Diagnosis*)

Our knowledge of motor, sensory, reflex, and visceral representation in the single segments of the cord, though far from what we would like it to be, is now sufficient to permit us tolerably sharply to localize circumscribed lesions involving any considerable amount of the white or gray matter at a definite level of the spinal cord. We have included, in a table, lists of the phenomena characteristic of involvement of the cervical, thoracic, lumbar and sacral portions of the spinal cord (see Gross Level Diagnosis), but there are 8 cervical, 12 thoracic, 5 lumbar and 5 sacral segments, besides 1 coccygeal segment. It becomes necessary, therefore, to make our localizing diagnosis still more precise by a consideration of the disturbances of motility, of sensibility, and of reflex and of visceral activity that result from the injury of each single segment of the cord, or of the anterior and posterior nerve roots pertaining to that segment (*segmental diagnosis, radicular topography*).

This segmental knowledge has come through a long series of embryological, anatomical, experimental physiological and clinical-pathological studies. The conditions in lower animals are much simpler than in man; for the human cord, our ideas of metamerism are based upon its relations to the anterior and posterior roots of each pair of spinal nerves. A segment of the spinal cord is, then, for clinicians, the immediate central projection of the anterior and posterior roots of one pair of spinal nerves. We assume that if one segment of the gray matter of the cord were destroyed, the sensory and motor symptoms would be topographically nearly

TABLE ILLUSTRATING GROSS LEVEL DIAGNOSIS IN LESIONS OF THE SPINAL CORD

| Part of Cord Affected | Motor Symptoms | Sensory Symptoms | Involvement of Reflexes | Involvement of Sphincters and Sexual Function | Trophic Disturbances |
|---|---|---|---|---|---|
| (*a*) Pars cervicalis (above the enlargement). This usually causes sudden death, but sometimes death is delayed for several days or weeks with paralysis of the diaphragm (N. phrenicus). ($C_1 - C_4$) | Spastic paralysis of arms and legs; atrophy of muscles supplied by upper cervical nerves. | Radiating pains in the domain of N. occipitalis major. | ..... | Loss of sensation of fullness of bladder and rectum; loss of voluntary control of sphincters; impotence. | Atrophy of muscles supplied by upper cervical nerves; decubitus. |
| (*b*) Intumescentia cervicalis (cervical enlargement). ($C_5 - Th_1$). | Spastic paralysis of the muscles of the lower extremities and trunk; partial, or complete, flaccid, atrophic paralysis of muscles of upper extremities. | Anesthesia of the lower extremities and of the trunk as high as the shoulders; partial, or complete, anesthesia of the upper extremities; hyperesthesias and pain in the latter. | Sometimes absent (total transverse lesion); if present, deep reflexes exaggerated; Babinski positive; sometimes oculopupillary symptom. ($Th_1$.) | Loss of sensation of fullness of bladder and rectum; loss of voluntary control of sphincters; impotence. | Atrophy and DeR. in muscles of upper extremities; often fever; decubitus. |
| (*c*) Pars thoracalis. ($Th_2 - Th_{12}$.) | Spastic paraplegia (lower extremities), with contractures. | Anesthesia of the lower extremities, and of part of the trunk, upper limit of trunk-anesthesia bounded sometimes by a zone of girdle-pain, or of objectively demonstrable hyperesthesia. | Sometimes absent; more often patellar clonus and ankle-clonus, with positive Babinski. | Loss of sensation of fullness of bladder and rectum; loss of voluntary control of sphincters; impotence (sometimes priapism or erections, on catheterization). | No marked atrophy; no DeR. in paralyzed muscles; decubitus; sometimes edema of the lower extremities. |
| (*d*) Intumescentia lumbalis (lumbar enlargement). ($L_1 - S_2$.) | Atrophic flaccid paralysis involving (according to level) muscles in domain of lumbar and sacral nerves. | Anesthesia of lower extremities reaching up to groins; no girdle pains; occasionally radiating pains in the legs. | Deep and superficial reflexes in lower extremities lost. | Marked paralysis of bladder and rectum, with incontinence; impotence. | Atrophy and DeR. in paralyzed muscles; decubitus. |
| (*e*) Conus medullaris. ($S_3 - S_5$; Coccyg.$_1$) | Motility in lower extremities completely retained. Paralysis of Mm. bulbi cavernosi et ischiocavernosi. | Anesthesia in the region of the anus, perineum, scrotum, penis and inner surface of thigh ("riding-breeches anesthesia.") | Loss of achilles reflexes on both sides. | Marked paralysis of bladder and rectum; abolition of spinal control of sphincter reflexes; usually total impotence; occasionally retention power of erection retained, with loss of power of ejaculation. | ..... |

the same as those that accompany destruction of the pair of Nn. spinales attached to that segment. The theory of Brissaud, according to which there is a metamerism in the cord in which parts of extremities (hand, forearm, upper arm, etc.) are definitely represented, is not now in favor; anatomical and clinical findings are not compatible with it.

We may most conveniently consider segmental diagnosis of diseases of the spinal cord by discussing (1) the segmental (or radicular) innervation of the body-musculature, (2) the segmental (or radicular) innervation of the skin, (3) the segmental (or radicular) representation of the more important spinal reflexes, (4) the segmental representation of the viscera, and (5) the combined representation of motion, sensation and reflexes in the single segments of the spinal cord. To this discussion we shall append a note regarding the topographical relations of the single vertebrae (1) to the segments of the spinal cord, and (2) to the points of emergence of the roots of the spinal nerves.

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### (*a*) *Segmental Representation of the Motor Functions* (*Myotomes*)

Knowledge here has been gained (1) by anatomical dissections (J. Müller, Herringham, Paterson, Bolk, Thorburn, Fröhlich and Grosser); (2) by embryological studies of developing neurotomes and myotomes (W. His, F. P. Mall, L. Bolk, Warren Lewis); (3) by histological studies of the cells in the cord by Nissl's method, (a) after section of nerves or extirpation of muscles (Marinesco, Parhon and Goldstein, Lapinsky); (b) after amputations (Flatau, Sano), or (c) after aplasias of muscle or nerve, or lesions of single nerves or muscles (v. Monakow, Parhon and Goldstein); (4) by experimental-physiological methods, stimulating the anterior roots and observing the muscular contractions that follow (Ferrier, Risien Russell, Sherrington); and by clinical-pathological methods, in which the

paralyses have been observed in instances in which the level of the lesion (tumor, myelitis, trauma) in the cord or anterior root has been established.

The peripheral motor nerve innervating a given muscle rarely, if ever, arises from a single segment, but, through the mediation of plexuses, has its origin in a combination of fibers from the anterior roots of several spinal nerves, that is, from several adjoining segments of the spinal cord. In other words, each muscle has a plurisegmental innervation. For the intercostal muscles only is the relation between the peripheral muscles and the spinal-cord segments more simple (unisegmental).

Again, a single anterior root may innervate, not only different muscles, but also muscles of different function. Furthermore, portions of a myotome may become innervated by the root more caudalward, or the root more cranialward, than that of the corresponding neurotome. Finally, in the innervation of the muscles of the extremities, the more proximal muscles are innervated by segments of a higher level than the segments innervating the more distal muscles (Herringham's law); thus the muscles of the hand are represented at a lower level ($Th_1$) than the level for the muscles of the shoulder ($C_4$-$C_5$).

In the accompanying tables, the segmental innervation of the body-musculature is graphically represented. In these tables the more proximal muscles of the extremities—that is, those nearest the spine—are generally placed above the more distal; that is, those further and further away from the spine are placed lower down. The segments of the spinal cord, from $C_1$-$S_5$ are presented as a continuous series passing from left to right. One can see at a glance the relation of the several muscles to the several segments (neurotomes).

A knowledge of the segmental distribution of disturbances of motility is of clinical importance for the correct localization of certain disease processes accessible to operation, which, without surgical interference, would be fatal. Among the diseases of this sort may be mentioned some obscure types of caries of the spine, pachymeningitis, serous arachnoiditis, and, especially, tumors of the vertebral column, of the meninges, and of the spinal cord.

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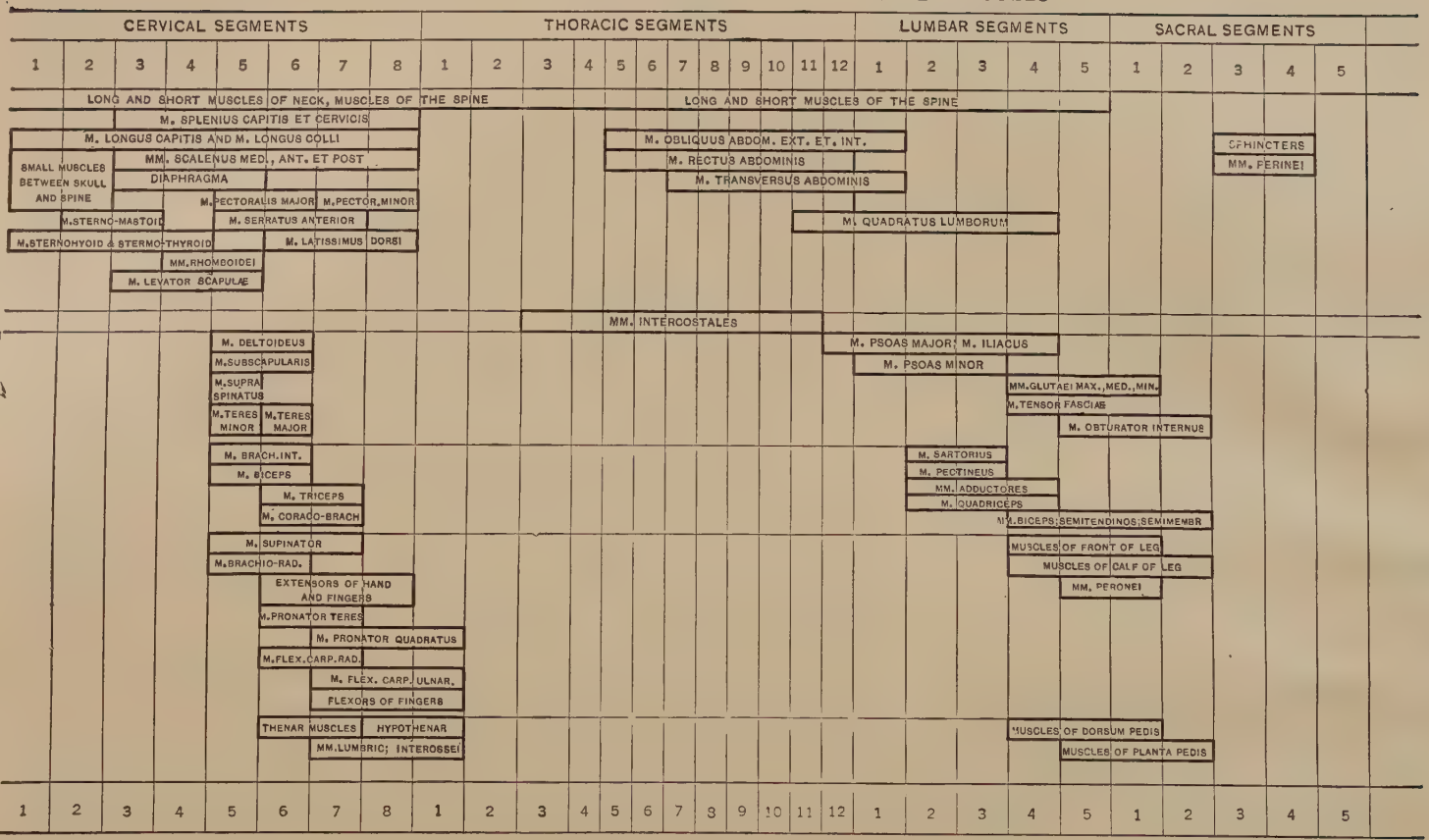
## SEGMENTAL INNERVATION OF THE PRINCIPAL MUSCLES


CERVICAL SEGMENTS
THORACIC SEGMENTS
LUMBAR SEGMENTS
SACRAL SEGMENTS
1 2 3 4 5 6 7 8 1 2 3 4 5 6 7 8 9 10 11 12 1 2 3 4 5 1 2 3 4 5
LONG AND SHORT MUSCLES OF NECK, MUSCLES OF THE SPINE
LONG AND SHORT MUSCLES OF THE SPINE
M. SPLENIUS CAPITIS ET CERVICIS
M. LONGUS CAPITIS AND M. LONGUS COLLI
SMALL MUSCLES BETWEEN SKULL AND SPINE
MM. SCALENUS MED., ANT. ET POST
DIAPHRAGMA
M. STERNO-MASTOID
M. PECTORALIS MAJOR
M. PECTOR. MINOR
M. SERRATUS ANTERIOR
M. STERNOHYOID & STERMO-THYROID
M. LATISSIMUS DORSI
MM. RHOMBOIDEI
M. LEVATOR SCAPULAE
M. OBLIQUUS ABDOM. EXT. ET. INT.
M. RECTUS ABDOMINIS
M. TRANSVERSUS ABDOMINIS
M. QUADRATUS LUMBORUM
SPHINCTERS
MM. PERINEI
MM. INTERCOSTALES
M. DELTOIDEUS
M. SUBSCAPULARIS
M. SUPRA SPINATUS
M. TERES MINOR
M. TERES MAJOR
M. BRACH. INT.
M. BICEPS
M. TRICEPS
M. CORACO-BRACH
M. SUPINATOR
M. BRACHIO-RAD.
EXTENSORS OF HAND AND FINGERS
M. PRONATOR TERES
M. PRONATOR QUADRATUS
M. FLEX. CARP. RAD.
M. FLEX. CARP. ULNAR.
FLEXORS OF FINGERS
THENAR MUSCLES
HYPOTHENAR
MM. LUMBRIC; INTEROSSEI
M. PSOAS MAJOR; M. ILIACUS
M. PSOAS MINOR
MM. GLUTAEI MAX., MED., MIN.
M. TENSOR FASCIAE
M. OBTURATOR INTERNUS
M. SARTORIUS
M. PECTINEUS
MM. ADDUCTORES
M. QUADRICEPS
M. BICEPS; SEMITENDINOS; SEMIMEMBR
MUSCLES OF FRONT OF LEG
MUSCLES OF CALF OF LEG
MM. PERONEI
MUSCLES OF DORSUM PEDIS
MUSCLES OF PLANTA PEDIS
1 2 3 4 5 6 7 8 1 2 3 4 5 6 7 8 9 10 11 12 1 2 3 4 5 1 2 3 4 5

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### (*b*) *Segmental Representation of the Sensibility of the Skin (Dermatomes)*

In the accompanying figures, the cutaneous areas innervated by the different segments of the spinal cord are graphically represented. It will be noted that the cutaneous areas innervated by segments of the thoracic cord run approximately horizontally, in girdle-shaped bands, around the trunk, while the areas innervated by cervical and lumbosacral segments (including the skin of the upper and lower extremities) are longitudinal zones that run more or less parallel to the long axis of these extremities. In the upper extremities these zones are nearly vertical; in the lower extremities they take a spiral course.

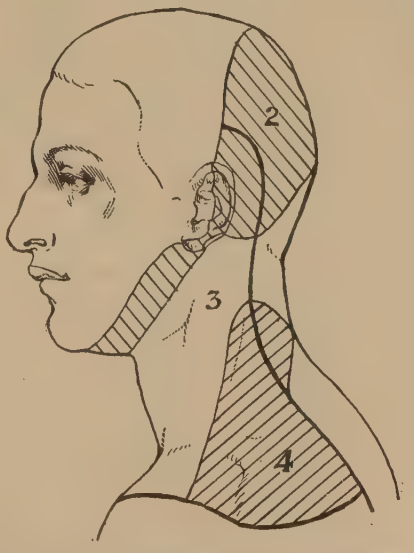


Fig. 577.—Arrangement of Dermatomes $C_2$-$C_4$. (After Bolk.)

We have pointed out already that the destruction of a single segment of the spinal cord does not cause a total anesthesia of the cutaneous area innervated by it, owing to the overlapping innervation from adjacent segments (Sherrington). A total anesthesia in a segmental domain indicates, therefore, involvement not only of that segment in the lesion, but also of two or more adjacent segments situated above and below it. The upper level of the lesion will be represented, therefore, not only by the segment whose cutaneous area is totally anesthetic, but by that higher segment whose cutaneous area shows only a hypesthesia; thus, for example, if the patient, on examination, were found to have a total anesthesia in the cutaneous domain corresponding to $Th_8$ in the figure, and only a hypesthesia in the domain corresponding to $Th_7$ and $Th_6$ in the figure, we would have to assume that the lesion in the spinal cord extends upward as far as the 6th thoracic segment.

Though it may be comparatively easy to establish very precisely the

situation of the upper level to which a lesion extends by a consideration of the sensory disturbances met with, the establishment of the lower level of that lesion may be impossible from a consideration of the sensory phenomena alone, owing to the fact that transverse lesions interrupting the

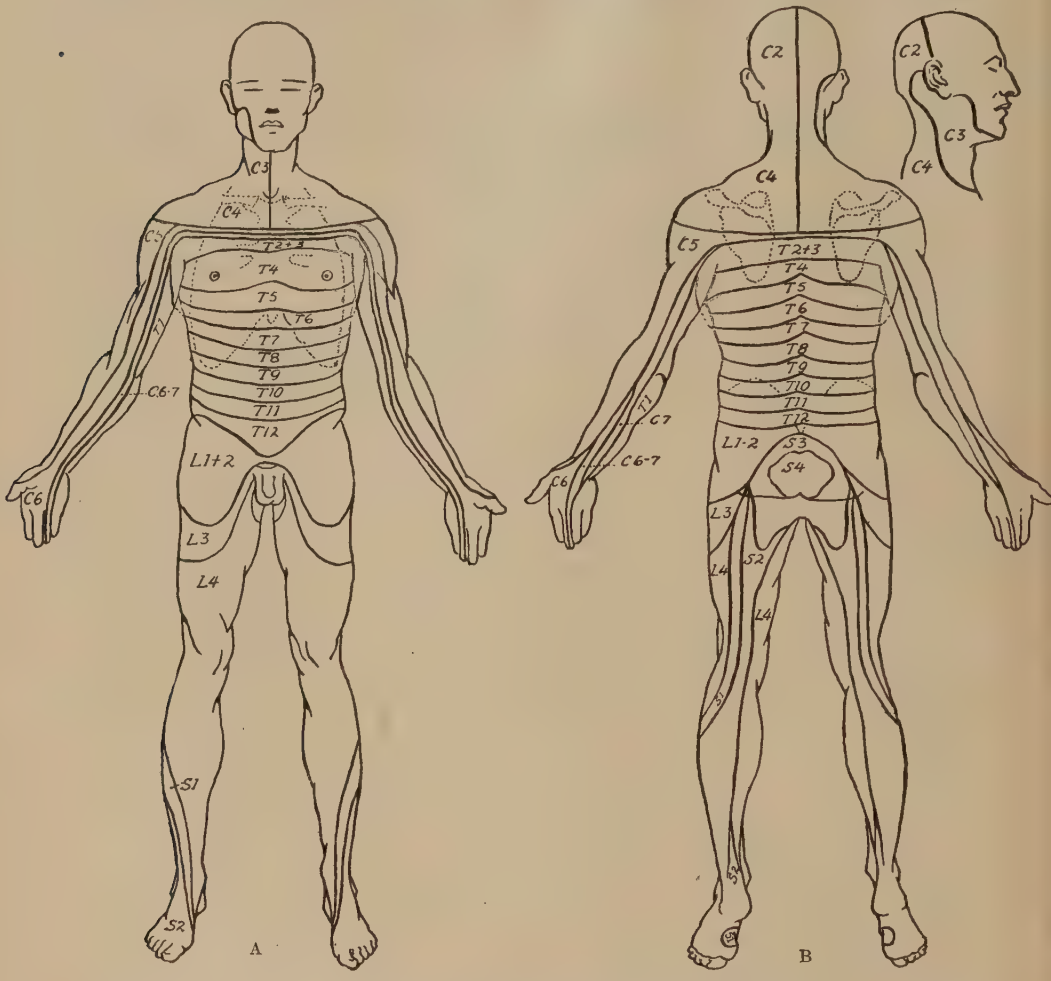


Fig. 578.—Segmental or Radicular Innervation of the Skin. A, Anterior Surface of Body; B, Posterior Surface of Body. (After Kocher.)

spinal cord at any given level injure not only the peripheral sensory neuron systems of the level itself, but they also, simultaneously, interrupt all the sensory conduction paths of the spinal cord carrying impulses upward to the brain from that portion of the body lying below the site of the lesion. A lesion completely interrupting the cord at the level of $Th_8$ causes, therefore, not only anesthesia in the cutaneous band (dermatome) correspond-

ing to $Th_8$, but of all the cutaneous bands (dermatomes) on the trunk below this, and of the whole skin of the lower extremities. The extent of an anesthesia is, therefore, often of great help in determining not only the upper segmental level of a lesion, but also the completeness of involvement in the transverse section of the cord at that level.

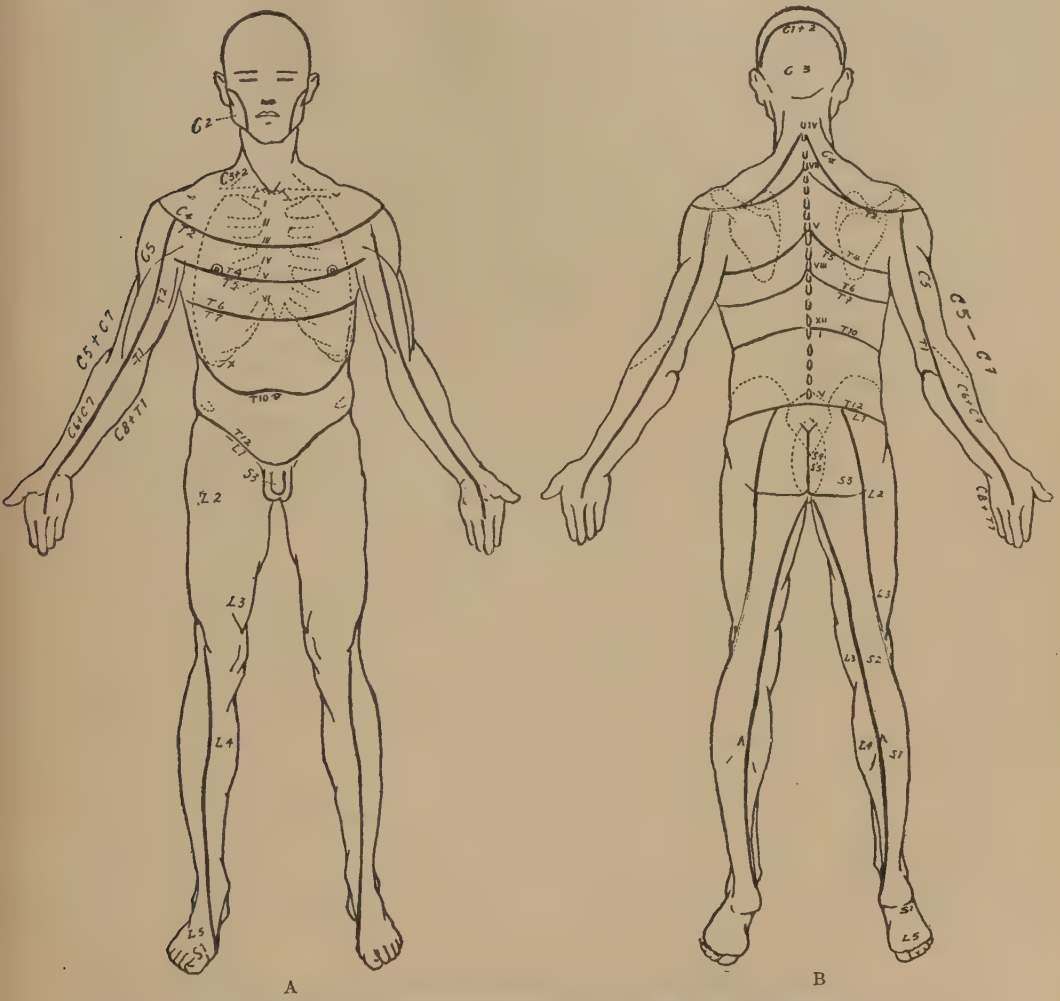


Fig. 579.—Direction Lines and Their Relations to Dermatomes and the Sensory Innervation of the Skin. A, Anterior Surface of Body; B, Posterior Surface of Body.

Some of the types of anesthesias depending upon total transverse lesions at certain levels of the lumbar and sacral cord are represented in the illustrations on page 416. Of course, in a transverse lesion, there is abolition of sensation, not only in the dermatomes supplied by the segment destroyed, but also in the dermatomes supplied by all the more caudally

situated segments, owing to destination of their paths, which pass upward in the white matter.

**Direction Lines.**—Recently, clinical attention has been directed to the relation of the dermatomes to certain *direction lines.* We distinguish between "primary" and "secondary" direction lines; thus, the lines limiting adjacent segments, for example, between $C_3$ and $C_4$, or between $C_5$ and $C_6$, are "primary limits," while the lines separating $C_5$, $C_6$ from $T_1$, $T_2$, and similar lines, are the so-called "secondary limits" (*differentiating limits* of Bolk; *ventral and dorsal axial lines* of Sherrington).

Eleven of these direction lines are of importance in clinical examinations (E. Flatau). They are as follows:

1. Soldier's vertex-ear-chin line. This is the upper boundary of the cervical domain. In front of it lies the domain of the N. trigeminus; behind it lies the sensory domain of $C_2$.
2. The neck-trunk limit, or cervicothoracic limit. This important line separates the cervical segments ($C_4$; $C_5$) from the thoracic segments ($Th_2$). Behind, this line separates $C_4$ from $Th_2$ in the lateral regions only. In the medial part, close to the spine, there is a triangle (for $C_5$-$C_7$), which separates $C_4$ from $Th_2$.
3. The cervicobrachial limit. This forms the boundary of $C_4$ and $C_5$ in the deltoid region.
4. The intermammillary line. In front, this lies between $Th_4$ and $Th_5$; behind, it crosses the lower angle of the scapula to reach the fifth thoracic spine.
5. The xiphoid line. This passes between $Th_8$ and $Th_7$; in front, it is at the level of the xiphoid process; behind, at the level of the eighth thoracic spine.
6. The umbilical line. This lies in front between $Th_9$ and $Th_{10}$ (Head and Campbell); behind, it corresponds to the level of the first lumbar spine.
7. The line between the trunk and the lower extremity. This lies between $Th_{12}$ and $L_1$. Behind, it is at the level of the first sacral vertebra. It runs lateralward, downward and forward below the crest of the ilium, and corresponds, in front, to a level just above the mons veneris.
8. Anterior axial line of the upper extremity. This corresponds, above, to the attachment of the first rib to the sternum (Bolk); it runs over the first intercostal space and the middle of the flexor surface of the upper arm and forearm to the middle of the wrist.
9. The posterior axial line of the upper extremity. This begins at the first thoracic spine, runs across the spine of the scapula, and down the middle of the extensor surface of the upper arm and of the forearm to the back of the wrist.
10. The anterior axial line of the lower extremity. This extends from the mons veneris close to the external genitals, down the middle of the median surface of the thigh to the medial condyle of the femur. It then turns backward to end about the middle of the calf, half way down the leg.
11. The posterior axial line of the lower extremity begins in the middle line at the first sacral vertebra, runs at first a little cranialward, and then down across the crest of the ilium and the great trochanter; thence it runs down the middle of the lateral surface of the thigh to the lateral condyle of the femur, then over the head of the fibula and forward and downward to end, in front, on the tibial crest, about its middle.

It will be noted that in the upper extremity the anterior and posterior axial lines separate segments $C_5$-$C_7$, which occupy the radial side, from segments $C_8$-$Th_2$, which occupy the ulnar side. Similarly, in the lower extremity, the two axial

lines in the thigh separate the lumbar from the sacral segments; on the whole, this is true, also, in the leg below the knee.

**Overlap of Innervation of Dermatomes.**—Sherrington's studies of the *overlap of the innervation of the dermatomes* is most important in clinical work. The overlap is more marked in some zones than in others; thus, in the hand, it is very pronounced, while in the trunk, the overlap is relatively slight. This overlap of the innervation of the dermatomes occurs in the longitudinal direction in the extremities.

The overlap for pain sensation is less than that for touch (Sherrington). This is why, on section of a single root of the brachial plexus, the touch anesthesia resulting is less than the analgesia; it is also in accord with the findings in herpes zoster. The dermatomes are, therefore like the, myotomes, plurisegmentally innervated, and we have pointed out above that, for this reason, in localizing diagnosis the upper limit of an anesthesia points to lesion of the next higher segment.

**Pre-fixed and Post-fixed Types.**—In making the segmental diagnosis from the topography of the anesthesia, the possibility of individual variations in the innervation of the dermatomes must be kept in mind. The variability may take the form of the "pre-fixed" or "post-fixed" type of Paterson; that is, a cutaneous zone may be supplied for half an area, or less, headward from its posterior root (pre-fixed type), or for half an area or less caudalward (post-fixed type). Such dislocations of the area have been observed by Head and Campbell in human cases. The post-fixation is usually bilateral, but may be unilateral (Sherrington).

**Segmental Anesthesias in Disease.**—Sensory disturbances with segmental, or radicular, topography are met with not only when a single segment or nerve root is the site of trauma, or disease, but also in certain organic diseases of the spinal cord. Among these, tabes, syringomyelia and hematomyelia are particularly prone to give rise to segmental disturbances of sensibility. Here the disturbance of sensibility may be confined to the dermatomes supplied by single segments, or groups of segments, and not involve all the more caudally situated dermatomes, as in the case of transverse lesions of the cord.

Thus in *tabes,* as has long been known (Oulmont), sensory disturbances are common in the mammillary and umbilical regions in front, and over the shoulder blades and over the small of the back behind. The girdle sensation of tabes is a well-known symptom, segmental in type. The tactile hypesthesia of the trunk in tabes affects most often the thoracic segments between the nipples and the umbilicus ($Th_4$-$Th_7$). When the sensory disturbance affects the upper and lower extremities, the anesthetic areas take the form of vertical, or spiral, bands corresponding to the segmental cutaneous zones we have described ($C_8$-$Th_1$; $L_5$-$S_1$). The analgesia, so often met with in early tabes on the back of the foot and toes, will be recognized as segmental in topography ($L_5$). These segmental disturbances in tabes have been especially studied by Laehr, Déjerine, and Patrick.

In many cases of *syringomyelia,* and of *gliosis spinalis,* the sensory disturbances (analgesia and thermanesthesia) are segmental in distribu-

tion; they depend then on destruction of the posterior horns of the gray matter of one or several segments.

In *hematomyelia* also, especially when it involves the conus or the

Fig. 580.—Herpes brachialis (Med. Service, J. H. H.)

epiconus, a similar topography of the disturbance of sensibility has been observed.

Finally, the lesions in *herpes zoster* correspond in their distribution to single dermatomes (Head and Campbell). This is said to be true also of the distribution of *naevi* (Klippel, Weil), and, in some instances, of *hypertrichosis* (Flatau).

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### (c) *Segmental Representation of the More Important Spinal Reflexes*

The reflex arc for the knee-kick is spread over at least three segments ($L_2$, $L_3$, and $L_4$) of the spinal cord, and their corresponding anterior and posterior roots; of these, $L_4$ is the most important for this reflex.

The ankle-jerk, or Achilles-reflex, appears to be represented in $L_5$, $S_1$, and $S_2$, especially in $S_1$.

The abdominal reflexes extend over the segments between $Th_8$ and $Th_{12}$; the supraumbilical reflex belongs to $Th_8$-$Th_9$, the infra-umbilical to $Th_{10}$-$Th_{12}$.

The plantar reflex arc is mediated by $S_1$-$S_2$, probably chiefly by $S_2$.

The cremaster reflex belongs to $L_1$ and $L_2$.

The vesical and rectal reflexes are represented by the segments between $S_3$ and $S_5$.

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### (d) *Segmental Representation of the Sympathetic Ganglia and of the Viscera Innervated by Them*

The white rami communicantes of each anterior root belong to the corresponding segment of the spinal cord. The relations of these to the

single vertebral and prevertebral ganglia of the autonomic system and the viscera they innervate have not yet been fully worked out. Among the points fairly well established may be mentioned the following:

1. The *vertebral ganglia,* with the exception of the superior cervical ganglion, supply the vascular innervation, the sweat-gland innervation and the pilomotor innervation of the *skin of the trunk and of the extremities;* the postganglionic fibers pass through a gray ramus communicans into the corresponding N. spinalis and are distributed among its peripheral branches.

2. The *skin of the head* (scalp, forehead, temples and cheeks) receive postganglionic fibers from the cervical sympathetic; the preganglionic fibers arise from $Th_1$-$Th_7$.

3. The *skin of the back* near the middle line gets its pilomotors from the thoracic vertebral ganglia.

4. The *upper extremities* get their sympathetic innervation from $Th_4$-$Th_{10}$, by way of the white rami communicantes, the truncus sympathicus, the ganglion stellatum, the gray rami communicantes and the plexus brachialis.

5. The segmental representation of the sympathetic innervation of the *skin of the lower extremities* is not yet well worked out.

6. Certain spinal nerves are devoid of pilomotors for the skin. This is especially true of $C_8$ and $S_1$. It is sometimes true also of $C_7$, $Th_1$, $S_2$, $S_3$.

7. In man the *anogenital blood vessels* (external genitals, anus, rectum) are represented in segments $S_2$-$S_4$.

8. The *sympathetic eye-supply* (smooth muscle of the eyelids, M. dilator iridis, secretory fibers of lacrimal gland) are derived from the superior cervical ganglion of the sympathetic; the preganglionic fibers come, in man, from $C_8$ and $Th_1$.

The more exact representation of vasomotility and of secretory function in the spinal cord has not yet been worked out.

9. The *visceral innervation from the prevertebral ganglia,* and its segmental representation in the spinal cord, is even less clear than the innervation of the smooth muscle and secreting glands of the skin by means of the vertebral ganglia. The prevertebral ganglia in the *celiac* plexus innervate the stomach, intestine, liver, spleen and pancreas; in the cat the preganglionic fibers come from the segments of the cord between $Th_5$ and $L_3$. The *inferior mesenteric ganglion* innervates the descending colon and the urogenital organs in the cat, the preganglionic fibers coming from the segments of the spinal cord between $L_1$ and $L_5$. The *ganglion stellatum* innervates the heart and the lungs, the preganglionic fibers come from segments $Th_1$-$Th_5$ (for the heart) and from $Th_3$-$Th_6$ (for the pulmonary blood vessels).

The representation of the sexual functions and the sphincters has been described elsewhere.

10. By the clinical method of studying the *pain referred to the dermatomes in visceral disturbance*, English investigators (Sturge, Allbutt, Ross, Mackenzie, Head) have drawn conclusions regarding segmental localization of the viscera in the spinal cord. According to Head's findings, the viscera are roughly represented in the cord as follows: Heart, [$C_{3-4}$; $Th_{2-8}$]; lungs, [$C_{3-4}$; $Th_{3-9}$]; stomach, [$C_4$; $Th_{7-9}$]; liver, [$C_{3-4}$; $Th_{7-10}$]; gall-bladder, [$Th_{8-9}$]; intestine, [$Th_{9-12}$]; testicle, [$Th_{10}$]; ovary, [$Th_{10}$]; kidney and ureters, [$Th_{10}$-$L_1$]; uterus, [$Th_{10}$-$L_1$]; prostate, [$Th_{10-12}$; $S_{1-3}$]; epididymis, [$Th_{11-12}$]; fallopian tubes, [$Th_{11}$-$L_1$]; urinary bladder (M. detrusor), [$Th_{11}$-$L_2$]; cervix of uterus, [$S_{2-4}$]; rectum, [$S_{2-4}$]; urinary bladder (mucous membrane and sphincter), [$S_{3-4}$].

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## (e) *Combined Representation of Motility, Sensibility and Reflexes in the Single Segments of the Spinal Cord*

In the tables on pages 411, 412, 413 and 414, will be found the most salient motor, sensory and reflex representations, corresponding to the various segments. Here are included only the points likely to be useful in clinical segmental diagnosis.

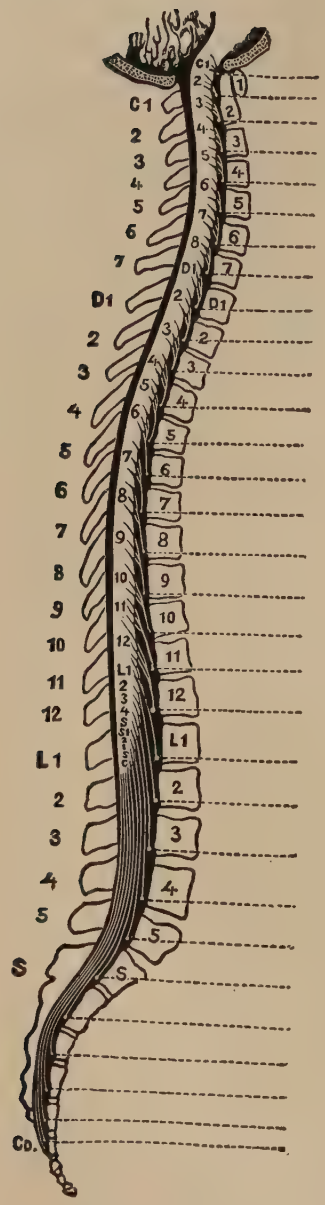


Fig. 581.—Gowers' Diagram, Illustrating the Topographical Relations of the Several Vertebrae to the Segments of the Spinal Cord and the Roots of the Spinal Nerves. (After W. R. Gowers.)

### (*f*) *Topographical Relations of the Vertebrae to the Segments of the Spinal Cord, and to the Level of Emergence of the Roots of the Spinal Nerves*

Though the spinal column extends from the foramen magnum to the coccyx, the upper end of the spinal cord lies midway between the atlas and the posterior margin of the foramen magnum, and the lower end of the spinal cord lies at the level of the spinous process of the first or second lumbar vertebra. The individual segments of the spinal cord, therefore, do not lie opposite the vertebra of the same name, and the spinal nerve roots, leaving the cord, traverse a longer, or shorter, distance before emerging from the spinal canal through the intervertebral foramina. The distance traversed increases as the caudal portion of the cord is approached. The lower portion of the vertebral canal, from the second lumbar vertebra on, contains only the nerve roots derived from the lumbar and sacral segments of the spinal cord—the so-called *cauda equina.*

In Gowers's diagram (Fig. 581), the relations of the individual segments of the spinal cord to the bodies and spines of the individual vertebrae are illustrated. Consultation of this figure is important for the surgeon who has to operate upon the spinal canal, since, after the lesion has been definitely localized in a given segment, or segments, it is necessary, in cases in which operation is indicated, to be able to expose that segment by performing laminectomy at a proper level. This is well illustrated in Finkelnburg's figure (Fig. 582). Assume that a neoplasm has given rise to a hypesthesia in the skin, the uppermost level of which belongs to the 7th thoracic segment of the spinal cord. This segment of the cord, as is seen in the figure, lies opposite the body of the 6th thoracic vertebra and the 5th

TABLE SHOWING SEGMENTAL REPRESENTATION OF MOTILITY, SENSIBILITY AND REFLEXES

| Segment of Spinal Cord; Spinal Nerve Roots | Muscles* | Movements | Cutaneous Sensibility† | Reflexes |
|---|---|---|---|---|
| $C_1$. | Small muscles of the neck. | Rotation and extension of the head. | | |
| $C_2$ and $C_3$. | 1. Muscles of the neck; M. sternocleidomastoideus;<br>2. M. trapezius. | 1. Flexion and rotation of the head;<br>2. Elevation of the shoulders. | $C_2$ Occiput; narrow strip along lower jaw; part of external ear;<br>$C_3$ "Sternomastoid zone." | |
| $C_4$. | 1. Mm. scaleni; diaphragm (N. phrenicus);<br>2. M. levator anguli scapulae. | 1. Costal and abdominal breathing;<br>2. Elevation of scapula. | (Head's sternonuchal zone.) 1. Dorsal part, quadrangular area of regio nuchae. 2. Ventral part, lateral region of neck; infraclavicular region, upper part of deltoid region, and part of suprascapular region. | Dilatation of the pupil on pinching the skin of the neck ($C_{4-7}$); |
| $C_5$. | 1. M. supraspinatus; M. infraspinatus; M. teres minor; Mm. rhomboidei;<br>2. M. deltoideus;<br>3. M. biceps; M. coracobrachialis; M. brachialis internus; M. brachioradialis;<br>4. M. supinator. | 1. Lateral rotation of upper arms;<br>2. Lifting upper arms;<br>3. Flexion of forearm;<br>4. Supination of forearm. | Small triangular area near the lower cervical spine; lateral surface of upper arm. | 1. Dilatation of pupil ($C_{4-7}$);<br>2. Scapular reflex ($C_5$–$Th_1$). |
| $C_6$. | 1. Mm. pectoralis major and minor; M. latissimus dorsi;<br>2. M. teres major; M. subscapularis;<br>3. M. serratus anticus major;<br>4. M. pronator teres;<br>5. M. triceps;<br>6. Thenar muscles. | 1. Adduction and depression of upper arm;<br>2. Medial rotation of upper arm;<br>3. Fixation and rotation of scapula;<br>4. Pronation of forearm;<br>5. Extension of forearm. | Small triangular area near lower cervical spine; radial surface of forearm and hand, including digits I–III. | 1. Dilatation of pupil ($C_{4-7}$);<br>2. Scapular reflex ($C_5$–$Th_1$);<br>3. Triceps reflex ($C_{6-7}$). |
| $C_7$. | Extensors of hand and fingers;<br>Flexors of wrist;<br>Thenar muscles. | Flexion and extension of the wrist. | Small triangular area near lower cervical spine.<br>Radial side of forearm and thumb; a small strip on the flexor surface of the forearm, and a longer strip on the dorsal surface lateral from the axial line. | 1. Dilatation of pupil ($C_{4-7}$);<br>2. Scapular reflex ($C_5$–$Th_1$);<br>3. Triceps reflex. ($C_{6-7}$);<br>4. Periostealradial reflex. |
| $C_8$. | 1. Long extensors and long flexors of the fingers;<br>2. M. pronator quadratus;<br>3. Hypothenar muscles. | Extension and flexion of the fingers. | Most of the hand and fingers (except the thumb on the volar surface, and the ulnar side of the little finger on the dorsal surface); small strips on front and back of wrist and forearm. | 1. Scapular reflex. ($C_5$–$Th_1$);<br>2. Palmar reflex ($C_7$–$Th_1$);<br>3. Ciliospinal reflex (efferent fibers) ($C_8$–$Th_1$). |

*For plurisegmental innervation of muscles see preceding table; here only the dominant segment is given.
†The names of the zones in quotation marks are those used by Head.

TABLE SHOWING SEGMENTAL REPRESENTATION OF MOTILITY, SENSIBILITY AND REFLEXES—Continued

| Segment of Spinal Cord; Spinal Nerve Roots | Muscles* | Movements | Cutaneous Sensibility† | Reflexes |
|---|---|---|---|---|
| $Th_1$. | 1. Hypothenar muscles;<br>2. Mm. interossei;<br>3. Mm. lumbricales. | ($C_8$ and $Th_1$). Movements of the thumb and fingers. | Medial surface of upper arm and ulnar edge of forearm and hand; part of little finger, the ring finger, and ulnar margin of middle finger.<br>"Dorso-ulnar zone." | 1. Scapular reflex ($C_5$–$Th_1$);<br>2. Palmar reflex ($C_1$–$Th_1$);<br>3. Cilio-spinal reflex (efferent fibers, ($C_8$–$Th_1$). |
| $Th_2$–$Th_{12}$. | 1. Muscles of the back;<br>2. Intercostal muscles ($Th_3$–$Th_{11}$);<br>3. Muscles of abdominal wall ($Th_5$–$L_1$). | 1. Movements of spine, extension and rotation;<br>2. Respiration;<br>3. Prelum abdominis; rising from recumbent position. | $Th_2$. Skin over thorax below the cervicothoracic limiting line (between 2d and 3d rib) lateralward to include the upper medial part of the arm; behind, to 7th cervical spine.<br>"Dorsobrachial zone."<br><br>$Th_3$. In front between 3d and 4th rib; behind, below the spina scapulae. To a slight extent in the axilla, and upper medial arm (?).<br>"Scapulobrachial zone."<br><br>$Th_4$. In front, region of nipples above the intermammillary line; behind, as low as 5th thoracic spine.<br>"Dorso-axillary zone."<br><br>$Th_5$. Area just below the nipples.<br>"Scapulo-axillary zone."<br><br>$Th_6$. In front, crosses xiphoid; behind, a little above 8th thoracic spine.<br>"Subscapulo-inframammary zone."<br><br>$Th_7$. In front, tip of xiphoid.<br>"Subscapulo-ensiform zone."<br><br>$Th_8$. In front about midway between nipple and navel.<br>"Mid-epigastric zone."<br><br>$Th_9$. In front, above the navel; behind, just above 1st lumbar spine.<br>"Supra-umbilical zone." | Upper abdominal reflex ($Th_{8-9}$). |

*For plurisegmental innervation of muscles see preceding table; here only the dominant segment is given.
†The names of the zones in quotation marks are those used by Head.

TABLE SHOWING SEGMENTAL REPRESENTATION OF MOTILITY, SENSIBILITY AND REFLEXES—Continued

| Segment or Spinal Cord; Spinal Nerve Roots | Muscles* | Movements | Cutaneous Sensibility† | Reflexes |
|---|---|---|---|---|
| | | | $Th_{10}$. In front, level of navel; behind, between 1st and 2d lumbar spines. "Subumbilical zone." | Lower abdominal reflex ($Th_{10-12}$). |
| | | | $Th_{11}$. In front, below the navel. "Sacro-iliac zone." | |
| | | | $Th_{12}$. In front, lowermost abdomen, above the direction-line separating the trunk from the lower extremity. "Sacro-inguinal zone." | |
| $L_1$. | 1. Lower abdominal muscles; 2. M. quadratus lumborum; 3. Mm. psoas major and minor. | 1. Prelum abdominis; 2. Lateral flexion of spine; 3. Flexion of thigh. | Skin of the groin. "Sacrofemoral zone." | Cremaster reflex ($L_{1-2}$). |
| $L_2$. | 1. M. ileopsoas; M. sartorius; 2. M. cremaster. | 1. Flexion of thigh; 2. Retraction of testicle. | Most of anterior surface of thigh; sensation in testicle and spermatic cord. "Gluteocrural zone." | 1. Cremaster reflex ($L_{1-2}$); 2. Knee-jerk ($L_{2-4}$). |
| $L_3$. | 1. M. ileopsoas; 2. Adductors of the thigh ($L_{2-4}$); 3. M. quadriceps ($L_{2-4}$). | 1. Flexion of the thigh; 2. Adduction of the thigh; 3. Extension of leg on thigh. | Region of the knee. | Knee-jerk ($L_{2-4}$). |
| $L_4$. | 1. M. quadriceps ($L_{2-4}$); 2. Lateral rotators of thigh; 3. M. tibialis anticus. | 1. Extension of leg on thigh; 2. Lateral rotation of thigh; 3. Dorsal flexion of foot; elevation of medial margin. | Medial surface of leg. | 1. Knee-jerk ($L_{2-4}$); 2. Gluteal reflex ($L_{4-5}$). |
| $L_5$. | 1. Mm. gluteus med. and min. ($L_4$–$S_1$); 2. M. semimembranosus; M. semitendinosus; M. biceps femoris. | 1. Abduction and medial rotation of thigh; 2. Flexion of leg. | 1. Narrow triangular area in front of ankle, extending to dorsum of foot; 2. Narrow triangular area over tendo-Achilles and heel, extending to planta pedis. "Fibulodorsal zone." | 1. Gluteal reflex ($L_{4-5}$); 2. Achilles-jerk ($L_5$–$S_2$). |
| $S_1$. | 1. M. gluteus maximus ($L_4$–$S_2$). | 1. Fixation of pelvis on thigh; extension of thigh. | 1. Narrow zone extending from the dorsum pedis up behind the fibula, on the lateral surface of the foot and leg; | 1. Achilles-jerk ($L_5$–$S_2$); |

*For plurisegmental innervation of muscles see preceding table; here only the dominant segment is given.
†The names of the zones in quotation marks are those used by Head.

TABLE SHOWING SEGMENTAL REPRESENTATION OF MOTILITY, SENSIBILITY AND REFLEXES—Continued

| Segment of Spinal Cord; Spinal Nerve-Roots | Muscles* | Movements | Cutaneous Sensibility† | Reflexes |
|---|---|---|---|---|
| | 2. M. pyriformis; M. obturator internus; Mm. gemelli; M. quadratus femoris; | 2. Lateral rotation of thigh; | 2. Narrow zone extending upward from behind the lateral malleolus; it extends in a spiral direction over the calf to reach the medial condyle of the femur. "Soleal zone." | 2. Plantar reflex ($S_{1-2}$). |
| | 3. M. tibialis anticus. Mm. peronei; Mm. extensor digitor. longus and brevis. | 3. Dorsal flexion of the foot and toes. | | |
| $S_2$. | 1. M. gastrocnemius; M. soleus; | 1. Plantar flexion of foot; | Lateral part of buttock, and most of posterior surface of thigh and upper lateral calf (anesthesia has riding-breeches shape). Lateral surface of leg; lateral margin of foot; sensibility of bladder and rectum. "Sciatic zone." | 1. Achilles-jerk ($L_5$–$S_2$); |
| | 2. M. flexor digit. comm.; M. flexor hallucis; | 2. Flexion of the toes; | | 2. Plantar reflex ($S_{1-2}$); |
| | 3. M. tibialis posticus; | 3. Adduction of foot, with elevation of its medial margin; | | 3. Ejaculation center ($S_{2-3}$). |
| | 4. Small muscles of foot. | 4. Flexion, abduction, and adduction of toes. | | |
| $S_3$. | 1. Perineal muscles; | Voluntary starting and stopping of urination and defecation; erection; second phase of ejaculation. | 1. Most of gluteal region; | 1. Ejaculation center ($S_{2-3}$); |
| | 2. Voluntary muscle of genito-urinary organs and rectum. | | 2. Perineum, scrotum, penis; 3. Uppermost part of medial surface of thigh. | 2. Erection center ($S_3$); 3. Bladder center ($S_{3-4}$); 4. Rectal center ($S_{3-4}$). |
| $S_4$–$S_5$ + coccyg. | 1. M. levator ani ($S_{3-4}$); | Voluntary starting and stopping of urination and defecation. | 1. Anal and perineal regions; | 1. Bladder centers ($S_{3-4}$); |
| | 2. M. sphincter ani externus ($S_{3-4}$); 3. M. coccygeus ($S_3$–coccyg.). | | 2. Medial sacral and coccygeal regions. | 2. Rectal centers ($S_{3-4}$); 3. Anal reflex ($S_5$ + coccyg.). |

*For plurisegmental innervation of muscles see preceding table; here only the dominant segment is given.
†The names of the zones in quotation marks are those used by Head.

thoracic spine. The surgeon would, therefore, begin to expose the tumor at the level of the 5th thoracic spine, and might have also to remove the 6th and 7th, and possibly also the 5th spine, since experience teaches that the site of the tumor more often has been assumed to be too low than too high.

Certain levels, it is especially helpful to keep in mind.

1. The junction of the cervical and the thoracic spine, or the level just beneath the eighth pair of cervical roots, corresponds to the interspace between the spines of the 5th and 6th cervical vertebrae.

2. The junction of the thoracic and lumbar portions of the spinal cord, or the level just beneath the 12th pair of thoracic roots, corresponds to the spine of the 9th thoracic vertebra.

3. The junction of the lumbar and sacral portions of the spinal cord, or the level just beneath the 5th pair of lumbar roots, corresponds to the spinous process of the 12th thoracic vertebra.

4. The level of the cord opposite the spine of the 1st lumbar vertebra is an important one; it corresponds to the position of the 3d, 4th and 5th sacral segments of the spinal cord.

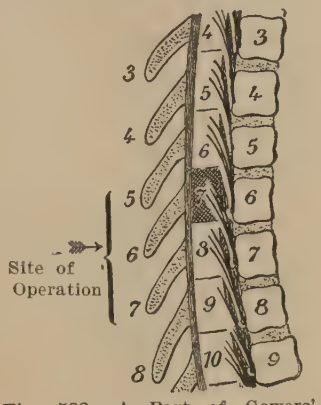


Fig. 582.—A Part of Gowers' Diagram (From 3rd to 10th Thoracic Vertebra) Showing the Relation of the Spinous Processes to the Bodies of the Vertebrae and the Relative Positions of the Segments of the Spinal Cord and the Vertebral Bodies. It Is Assumed that there Is a Lesion of the 7th Thoracic Segment of the Spinal Cord. (After Finkelnburg in P. Krause's "Lehrb. d. klin. Diagnostik inner. Krankh.," published by G. Fischer, Jena.)

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## (*g*) *Differential Diagnosis of Lesions of the Lumbar Enlargement, the Conus medullaris, and the Cauda equina*

Owing to the fact that the anterior and posterior roots of the lumbar and sacral nerves, after emergence from the spinal cord, run inside the vertebral canal, downward, for some distance, close beside one another, we sometimes encounter great difficulty in definitely localizing the lesion; for it is obvious, that a lesion of the cauda equina in the region of the lower lumbar or sacral vertebrae may give rise to a group of symptoms very similar to those that follow upon a focal lesion at the level of the lumbar enlargement. By consulting Fig. 583, it will be seen that a lesion at (A), at the level of the 12th thoracic vertebra, involving the spinal cord (but not the adjacent N. femoralis) will give rise to the same motor and sensory disturbances in the domain of the N. ischiadicus, as a lesion

at (B), in the cauda equina, situated below the level of exit of the N. femoralis (*N. cr.*).

In differentiating between lesions of the *lumbar enlargement* and lesions of the cauda, therefore, we have to consider, in addition to these motor and sensory symptoms, (1) accompanying phenomena referable to lesions in the spinal column itself (history of trauma, x-ray examination,

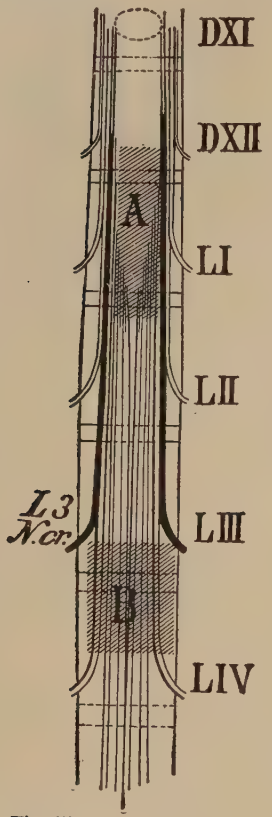


Fig. 583.—Diagram of the Vertebral Column with the Lower Portion of the Spinal Cord and the Cauda equina. A, Lesion at the Level of the Lower Part of the Spinal Cord Just Below the 12th Thoracic Vertebra. B, Lesion at the Level of the 3d Lumbar Vertebra Involving the Cauda equina. (After Schultze.)

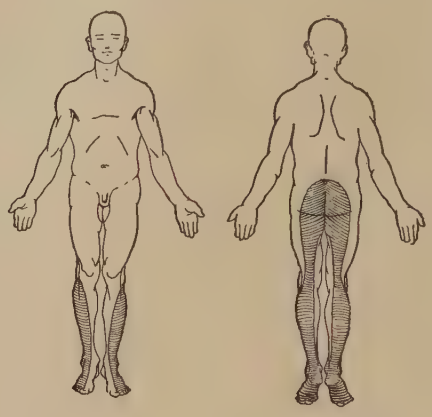

Fig. 584.—Lesion in the Region of the 5th Lumbar Segment.

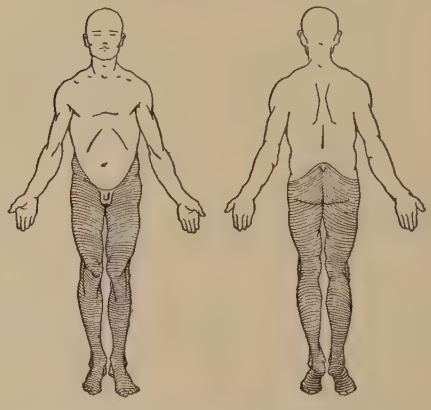

Fig. 585.—Lesion in the Region of the 2d Lumbar Segment.

local tenderness, etc.), and (2) the serial sequence of the single symptoms, and the rapidity with which they develop. Tumors of the *cauda equina* more often cause unilateral symptoms, and are more frequently associated with severe radiating pains; and they are less often accom-

panied by fibrillary twitching than are tumors, or other lesions, in the region of the lumbar enlargement.

A similar difficulty exists in the differential diagnosis between diseases of the conus (segments $S_{3-5}$), and diseases of the cauda equina. In pure *conus* lesions, there is paralysis of the rectum and bladder, loss of the sexual reflexes and of the ankle jerk, without paralyses in the muscles of the lower extremities. Riding-breeches anesthesia may be due either to conus lesion, or to a localized cauda-lesion involving only the root-fibers of the conus in the sacral part of the vertebral canal. Conus-lesions are practically always bilaterally symmetrical. Dissociation of sensation is common in conus-lesions, rare in cauda-lesions. There is rarely spontaneous pain in conus-lesions; in lesions of the cauda, violent neuralgias in the regions of the sacrum, perineum, bladder, rectum, and along the sciatic nerve are characteristic.

The *epiconus* (Minor) includes the segments $L_5$–$S_2$. When these segments are injured, the muscles innervated by the sacral plexus undergo degenerative atrophy. The Mm. peronei are especially involved and the Mm. glutei may atrophy; but the M. tibialis anterior may escape. If the process be limited to the gray matter of the epiconus, the Achilles-reflex is abolished, but the knee-kick can be elicited and the sphincters remain unaffected.

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# D. Topical Diagnosis of Lesions of the Medulla Oblongata and Pons (Rhombencephalic Lesions)

## 1. Anatomical Physiological Preliminaries

A knowledge of the anatomy and physiology of the medulla and pons gives the clues for the recognition of disturbances of function due to lesions situated here.

In the medulla and pons, groups of cell-bodies of lower motor neurons are isolated in single masses known as the *nuclei of origin of the motor cerebral nerves* (nuclei of Nn. XII, XI, X, IX, VII, VI, V). The sensory roots of the cerebral nerves, correspond to the posterior root fibers of the spinal nerves. They enter at various points. Some of them terminate upon masses of gray matter (so-called *nuclei of termination of the sensory cerebral nerves*), which correspond

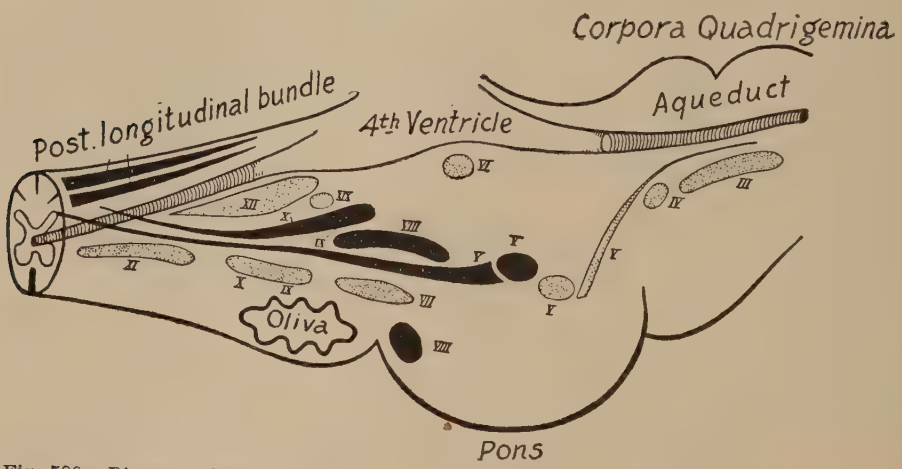


Fig. 586.—Diagram of Nuclei of Cerebral Nerves III-XII. Motor Nuclei Stippled; Sensory Nuclei Black. (After Villiger in M. Rothmann's article in "Handb. d. inn. Med.," published by J. Springer, Berlin.)

to the gray matter of the posterior horns of the spinal cord. Others extend for some distance longitudinally within the central system, finally to terminate in more distant gray matter; these latter fibers correspond to the posterior funiculi of the spinal cord, which terminate in the nuclei of Goll and Burdach.

In the formatio reticularis, there run, from these various nuclei of termination of the sensory cerebral nerves, *sensory neurons of the second order*, which carry impulses (1) to the cerebellum, and (2) to the cerebrum; the latter are, for some distance, separated from the similar fibers that conduct impulses upward from the cord.

In addition, in the medulla and pons, the great bundles of fibers of the *motor conduction paths* (corticonuclear path to the motor cerebral nerves; pyramidal tracts passing toward the spinal cord)—all axons of upper motor neurons—run downward, ventrally, on each side of the middle line. Of these, the fibers going to the nuclei of the cerebral nerves cross at different levels; those going to the

nuclei of N.III and N.IV have already crossed in the midbrain; those going to the motor nucleus of N.V cross in the upper part of the pons; those going to the nuclei of N.VI and N.VII cross at about the middle of the pons; those going to the motor nuclei of N.IX, N.X and N.XII cross at successively lower levels in the medulla oblongata. At a still lower level in the medulla oblongata is situated the main *decussation of the pyramids* (decussatio pyramidum); in these pyramids are contained the axons of the upper motor neurons going to the anterior-horn cells of the spinal cord, the crossed fibers going through its lateral funiculus as the fasciculus pyramidalis lateralis, the uncrossed fibers going down in the anterior funiculus as the fasciculus pyramidalis anterior. (See Fig. 589, p. 438.)

The great *afferent, or general sensory, conduction path* also presents certain definite features in the pons and medulla that must be kept carefully in mind. The posterior funiculi of the spinal cord (uncrossed axons of peripheral sensory neurons) end in the nuclei of Goll and Burdach at the lower end of the medulla oblongata. These fibers carry homolateral impulses of deep sensibility and touch. The neurons of the second order, with cell-bodies in the nuclei of Goll and Burdach, give off axons that form the internal arcuate fibers, which undergo decussation at the raphe of the medulla (*sensory decussation* or decussatio lemniscorum) and then run forward in a compact bundle on each side as the interolivary layer of the lemniscus, and higher up in the pons as the *lemniscus medialis* or "medial fillet." They are on their way to terminate, chiefly, in the ventrolateral nuclei of the thalamus.

There are also sensory neurons of higher order that carry the impulses of *pain sense and temperature sense* from trunk and extremities; their path is already crossed in the spinal cord. The fibers are continued upwards in the medulla oblongata in the ventrolateral portion of the formatio reticularis. Some fibers for the sense of touch lie in the formatio reticularis a little medial from these. Higher up in the pons, these fibers, in all probability, become more closely related spatially to the fibers carrying impulses of deep sensibility (in the lemniscus medialis). The sensory neurons of the second order from the cerebral nerves also form conduction paths, not yet well localized by the histologists. There is evidence that they run, at first, separate from the spinal fibers and that, later, they join them in the upper portions of the lemniscus medialis. An exception, however, must be made for the sensory neurons of the second order of the *cochlear path*. These run, first, in the corpus trapezoideum (crossing of the fibers) and in the striae acusticae, and then form a compact bundle, on the opposite side, known as the *lateral lemniscus*, or "lateral fillet," which runs upward to terminate, partly in the inferior funiculus of the corpora quadrigemina (acoustic reflex mechanism for movement of the head and eyes), and partly in the medial geniculate body, where a new neuron system starts, which carries impulses thence to the acoustic sense area in the cortex of the temporal lobe. A part of the cochlear path runs up on the same side.

In addition to the neuron systems already mentioned, the medulla and pons are most intimately related with the cerebellum by means of its three pairs of cerebellar peduncles. The inferior cerebellar peduncle (*corpus restiforme*) in the pons, carries mainly centripetal neurons of the second order (continuations of direct cerebellar tract and other spinocerebellar tracts concerned in muscular coördination). The middle cerebellar peduncle (*brachium pontis*) carries fibers connecting the nuclei of the pons with the cerebellum; and the superior cerebellar peduncle (*brachium conjunctivum*) carries fibers connecting the cerebellum (especially the nucleus dentatus) with the red nucleus and the cerebral cortex of the opposite side, the crossing occurring just caudal from the red nuclei in the decussatio brachii conjunctivi. This superior cerebellar peduncle carries impulses

in both directions, so that, through it, the so-called voluntary activities of the cerebral cortex are modified by the regulatory or *coördinating activities* of the cerebellum. The functions of the cerebellum are to a large extent subordinated in turn to the activities of the cerebral cortex, partly through cerebellopetal impulses arriving through the superior peduncles, more largely through cerebellopetal impulses derived from collaterals of the pyramidal-tract fibers to the nuclei pontis and thence passing through the middle peduncle into the cerebellum.

In the rhombencephalon, the very important *vestibular mechanism* has its seat. Through Deiter's nucleus, which receives impulses from the vestibular nerve, on the one hand, and the cerebellum, on the other, and gives off a descending path that goes to the anterior-horn cells of the spinal cord, the tonic innervation of the musculature is in all probability kept up, and the regulatory, coördinating influence of the cerebellum on the movements of the extremities and trunk (see "pointing-error" tests) is mediated. From the vestibular apparatus, also, go fibers into the *medial longitudinal bundle* (fasciculus longitudinalis medialis), an association-path connecting, and coördinating, the activities of the eye-muscle nuclei with the nuclei governing the muscles of the head; through it the associated movements of the eyes and head are regulated, and injury to it may cause conjugate deviation, nystagmus and other phenomena (See Vestibular Syndromes).

In the formatio reticularis of the medulla oblongata and pons are situated also certain groups of neurons of the highest importance for the internist; these are the so-called *vital centers,* namely, the respiratory neuronal mechanism, the cardio-inhibitory mechanism, the general vasomotor center, the center governing deglutition, that governing phonation, etc.

## 2. Tetraplegia; Hemiplegia cruciata; Hemiplegia alternans

All these structures, local and conducting, are crowded together into a very narrow space, so that a small lesion of the medulla or pons, whether it be unilateral or bilateral, may produce large effects. Thus, in the medulla oblongata, a small lesion may involve a pyramid and cause paralysis of the opposite arm and leg, or both pyramids simultaneously, causing paralysis of all four extremities (*tetraplegia*). In one situation in the medulla a lesion will paralyze the arm of the opposite side and the leg of the same side (*hemiplegia cruciata*).

Most lesions of the medulla oblongata proper (or so-called bulbar lesions), whether they involve the other motor and sensory paths or not, cause some injury to the nuclei of origin or of termination of the cerebral nerves arising or ending in it (N.XII, N.XI, N.X, N.IX) or to their roots, and cause dysarthria, aphonia, disturbances of deglutition, or taste. According as the paralysis of the tongue is due (1) to lesions of the lower motor neurons (nucleus N. hypoglossi, or radix N. hypoglossi), as is usually the case in bulbar lesions, or (2) to lesions of the upper motor neurons (corticonuclear path), DeR with atrophy in the muscles of the tongue will, or will not, be present.

Focal lesions in the uppermost part of the pons, above the level where

the corticonuclear fibers of the pontile and bulbar motor nuclei cross, give rise to *hemiplegia* of the opposite side of the body (upper-motor-neuron paralysis), and, sometimes, to *hemianesthesia* of the opposite side (lemniscus lesion).

Among the most interesting focal lesions of the pons and medulla are those causing a *hemiplegia alternans,* that is, a homolateral paralysis in the domain of a cerebral nerve along with a contralateral hemiplegia. Thus, if a lesion in the pons is situated at, or just above, the level of the nucleus N. facialis, then the through motor path of the upper motor neurons (corticonuclear path to N.IX, X, XI, XII; pyramidal tract to opposite arm and leg) may be involved, simultaneously with involvement (a) of the corticonuclear fibers to the facial nucleus after they have crossed the raphe, (b) of the nucleus N. facialis itself, or (c) of its root (radix N. facialis); in such cases, there will be a paralysis of the face on the side of the lesion, and of the extremities and the tongue upon the opposite side of the body. This form of hemiplegia, the Millard-Gubler type of hemiplegia alternans, or *hemiplegia alternans inferior,* is highly characteristic of lesions in the pons. The facial paralysis is then usually a flaccid, degenerative paralysis owing to the involvement of the nucleus N. facialis or the radix N. facialis (lower-motor-neuron lesion); occasionally, however, the facial paralysis is a simple, non-atrophic paralysis like that of the arm and leg on the opposite side due to the fact that, in rare instances, the lesion has injured, not the nucleus itself or the nerve root, but the corticonuclear fibers after they have crossed the middle line (raphe) and just before they have terminated in the nucleus N. facialis (supranuclear facial paralysis; upper-motor-neuron lesion). (Of course if these supranuclear facial fibers are injured before they cross, the facial paralysis will be on the same side as the paralysis of the arm and leg.)

Other forms of hemiplegia alternans may occur in focal lesions of the pons and medulla; thus we may have a paralysis of N.V, N.VI, N.IX, N.X, or of N.XII of the same side, along with paralysis of the arm and leg on the opposite side (*hemiplegia alternans infima*).

One especially interesting type of hemiplegia alternans is that in which a focal lesion causes paralysis of the associated lateral movements of the eyes toward the side of the lesion, facial paralysis on the side of the lesion and contralateral paralysis of the arm and leg (*Foville's type of hemiplegia alternans*). It is obvious that this type differs from the Millard-Gubler type in the addition of associated lateral eye-movement paralysis (due to injury to the medial longitudinal bundle or to the pontile center for associated lateral movements of the eyes). In some cases, the facial paralysis may be contralateral, like the paralysis of the extremities. Other forms of hemiplegia alternans occur with lesions of the midbrain (*q. v.*).

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## 3. Hemianesthesia cruciata

Occasionally, in a lesion of the upper lateral region of the medulla oblongata, involving the tractus spinalis N. trigemini along with part of the corpus restiforme, the fibrae arcuatae internae, the nucleus ambiguus, and the upward continuation of Gowers' tract, a crossed hemianesthesia (*hemianesthesia cruciata*) is met with; there is anesthesia and areflexia of the face of the same side, and of the arm, trunk and leg of the opposite side; the disturbance of sensibility in the arm and leg usually shows a dissociation (analgesia and thermanesthesia only). Sometimes there is homolateral bathyanesthesia with ataxia and slight tactile hypesthesia. This lesion is most often due to embolism or thrombosis of the posterior inferior cerebellar artery. Dysphagia, dysphonia and singultus may be temporary symptoms (H. M. Thomas, W. G. Spiller, Gordinier, Wallenberg, Marburg and Breuer).


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## 4. Bilateral Lesions of the Pons and Medulla

Bilateral lesion of the medial longitudinal bundle, or its neighborhood, can cause bilateral paralysis of the associated movements of the eye muscles.

Bilateral lesions of the pons causing paralysis of all four extremities are usually associated with bilateral involvement of the corticonuclear paths of the motor cerebral nerves, resulting in a supranuclear, non-degenerative bulbar paralysis with disturbance of speech and deglutition. Similar lesions in the medulla oblongata are prone to involve the nuclei of the cerebral nerves rather than to be supranuclear and they cause degeneration of the tongue; they are further distinguished from pontile lesions by the integrity of the functions of the pontile motor nerves (motor part of N.V; N.VI; N.VII).

Focal lesions in the pons are most often due to softening from thrombosis. Hemorrhages are rare, but they do occur; I have more than once seen them at autopsy.

The cell-bodies of the nuclei of the motor nerves in the pons and medulla are not infrequently involved in poliencephalitis (corresponding to poliomyelitis anterior in the cord). In multiple sclerosis there are nearly always nodules in the pons.

The motor nuclei of the medulla and pons are also involved in progressive bulbar paralysis and in amyotrophic lateral sclerosis; not infrequently a progressive muscular atrophy beginning in the extremities extends to the motor nuclei of the bulb.

The medulla oblongata and pons are also frequently subjected to compression, especially in tumors of the base of the brain and cerebellum, in lues, and in aneurisms of the vertebral and basilar arteries. In pseudobulbar paralysis (*q. v.*) it is the supranuclear motor paths, or corticonuclear axons of the upper motor neurons, that are involved, somewhere between the cerebral cortex and the nuclei of origin of the motor cerebral nerves. In myasthenia gravis (*q. v.*) we have to deal with a bulbar paralysis without known anatomical basis.

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# E. Topical Diagnosis of Lesions of the Cerebrum

The cerebrum includes the *midbrain* or mesencephalon, the *interbrain* or diencephalon, and the *end brain* or telencephalon. We shall consider (1) certain general symptoms pointing to involvement of the cerebrum, and (2) symptoms pointing to each of these three main portions of the cerebrum separately.

## 1. General Cerebral Symptoms

Certain general cerebral symptoms are due to an increase of intracranial pressure, following upon an increase of the cerebrospinal fluid or upon the presence of some abnormal space-occupying mass, within the skull-cavity. They represent, in part, interference with the functions of the cerebrum itself, in part injury to other parts of the brain (cerebellum, pons, medulla oblongata). They include: (1) choked disk, (2) headache, (3) dulling of consciousness, (4) vomiting, (5) vertigo, (6) bradycardia, (7) general convulsions, and (8) in meningeal irritation, rigidity of the neck.

As long as these general symptoms alone exist, great caution should be exercised in diagnosis, for, while they may indicate the presence of an organic disease of the brain (*e. g.*, brain-tumor), it must not be forgotten that several of them, like headache, vomiting, dulling of consciousness, and general convulsions, may be due (a) to intoxications of the brain (*e. g.*, uremia, alcoholism, lead-poisoning), (b) to

general infection (septicemia, scarlet fever, typhoid), or (c) to local infections (meningitis, encephalitis). Even the presence of choked disk, or neuritis optica, does not necessarily indicate the presence of a brain-tumor; for this condition may be met with in atherosclerosis, in nephritis, in chlorosis, in multiple neuritis, and in saturnine encephalopathy.

Now, while it is true that these general cerebral symptoms may be secondary, and not due to a primary organic disease of the brain, it is also true that a real organic disease of the brain may for a long time cause only single subjective symptoms like vertigo, or headache. Not infrequently in such cases, the diagnosis of a psychoneurotic state (psychasthenia; neurasthenia; hysteria) is erroneously made, when in reality we have before us a beginning brain-tumor, a cerebral atherosclerosis, or some other form of organic cerebral disease. In all such cases, it is well to hold the mind open until observation, over a considerable period, has shown the absence of any progression of the cerebral symptoms, or the persistent absence of objective symptoms like choked disk and of definite focal symptoms.

## 2. Focal Cerebral Symptoms

For localizing purposes, and for the definite diagnosis of organic diseases, the recognition of focal symptoms, that is, of symptoms that point to lesion of definite areas in the brain are most important. Organic disease of the brain may exist, as we have already said, for a long time without the appearance of such focal symptoms, especially if the so-called *silent areas* are first involved, but, sooner or later, if the disease be progressive, symptoms will usually appear, (1) through direct extension of the pathological process to the non-silent areas (*focal symptoms*), (2) through action of the disease in the silent areas upon the neighboring non-silent areas (*neighborhood-symptoms*), as when, for instance, a disease, beginning in the nucleus caudatus or in the thalamus, causes no symptoms until the adjacent internal capsule is pressed upon and causes disturbances of motility or sensibility like those that are due to a primary lesion of the internal capsule, or (3) through action at a distance owing to the loss of certain components of the distant function normally supplied by the cerebral substance injured by the focal lesion (*diaschisis-symptoms* of v. Monakow).

The symptoms due to diaschisis are dynamic in origin like the symptoms due to *shock*. If a piece of intestine or the stomach be crushed, the symptoms extend far beyond the neuron complexes directly injured; violent centripetal impulses are set up, which affect deleteriously groups of neurons far removed from the site of the injury; serious symptoms (cardiac, respiratory, vasomotor, secretory) appear in the form of general prostration with psychic disturbance. The disturbances in shock are severe but transitory; the patient either dies or he recovers quickly. The action at a distance after a lesion of the central nervous system is somewhat different. Thus, after a cerebral hemorrhage, the knee-jerks may disappear entirely for some time. Or, with a lesion in the left hemisphere,

not *directly* involving the speech areas at all, there may be, at first, severe aphasic disturbances. Again, with a very small destructive lesion in the speech areas, there may be severe speech disturbance at first, and, later, all will disappear except a slight residual defect. Thus, after a central focal lesion, the neurons at a distance connected with the neurons destroyed cease temporarily to function or show diminished function (*phenomena of diaschisis*); later, the distant function may be restored in whole or in part through adaptation, the dynamic disturbance disappearing ("wearing off" of the diaschisis). There is a good deal of difference of opinion as to how far we may justifiably apply v. Monakow's doctrine of diaschisis in explaining nervous symptoms.

By *focal lesions of the cerebrum,* we mean those that are not diffuse, but are circumscribed, involving certain areas (foci) only. A focal, or circumscribed lesion, if it affect a silent area, may not cause symptoms, but when the focus is in a non-silent area, symptoms of disturbance of motility, of cutaneous or deep sensibility, of the special senses, of speech, of writing, etc., will appear; these symptoms are called "focal symptoms."

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## 3. Lesions of the Midbrain (Mesencephalon)

The midbrain, though anatomically a part of the cerebrum, is perhaps more closely related in structure to the pons and medulla. It is divisible into two parts: (1) that lying dorsal from the level of the aqueductus cerebri, known as the corpora quadrigemina, and (2) that lying ventral from it, known as the cerebral peduncle (pedunculus cerebri).

The *corpora quadrigemina* consist of four "hillocks," the two upper ones (*superior colliculi*) being (1) an optic reflex center, and, to a certain extent, perhaps,

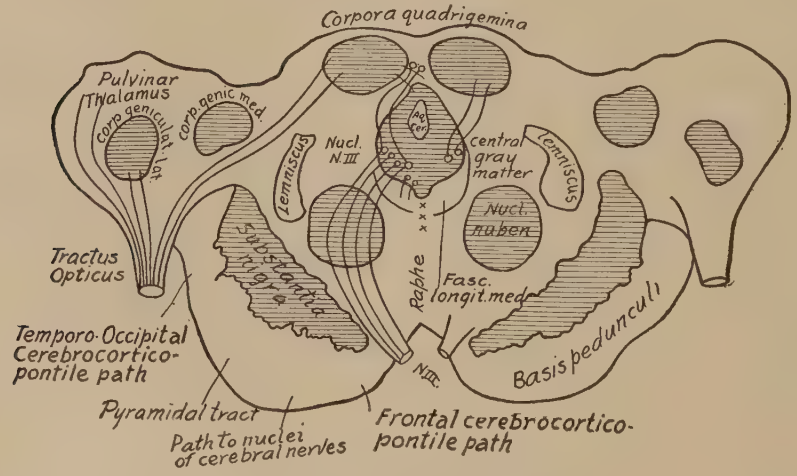


Fig. 587.—Diagram of Section Through the Midbrain, at the Level of the Corpora quadrigeminus and the Cerebral Peduncles.

(2) concerned in visual acuity for central vision; the two lower hillocks (*inferior colliculi*) are acoustic reflex centers.

Each *cerebral peduncle* consists of two parts, (1) a dorsal part, or tegmentum, and (2) a basal part (basis pedunculi), sometimes called the "foot of the cerebral peduncle," or pes pedunculi.

The tegmentum and basis are separated from one another by the substantia nigra.

In the *tegmentum,* there is a mass of gray matter surrounding the aqueductus cerebri, known as the "central gray matter," in which are situated, on each side,

the nuclei of the third and fourth cerebral nerves (nucleus N. oculomotorii; nucleus N. trochlearis), the latter lying caudalward from the former. Beneath these nuclei, on each side, lies the medial longitudinal bundle (fasciculus longitudinalis medialis), an association path connecting the eye-muscle nuclei and the motor nuclei of the head and neck with one another, and associating their activities.

In the middle of the tegmentum, on each side, lies the red nucleus (nucleus ruber), an important way station in the path that runs both ways between the cerebellum and the opposite cerebral cortex through the superior cerebellar peduncle (brachium conjunctivum). Lateral from and above the red nucleus, on each side, lies the medial lemniscus or "fillet" (main sensory path to the cerebrum), and still further lateralward and upward lie the geniculate bodies (really in the diencephalon), the medial one receiving the lateral lemniscus with its cochlear (acoustic) impulses, the lateral one receiving the optic tract with its optic (visual) impressions.

From some of the cells of the nucleus ruber arise the fibers of von Monakow's bundle, which crosses in Forel's tegmental decussation and then runs downward on the opposite side in the formatio reticularis of the pons into the medulla oblongata ventral from the tractus spinalis nervi trigemini and thence into the lateral funiculus of the spinal cord (ventral from the lateral pyramidal tract) to end in the anterior horns. This bundle is known as the tractus rubrospinalis and is regarded as one of the more important of the extrapyramidal, or parapyramidal, motor paths.

The *basis pedunculi* or foot of the peduncle (pes) lies below the substantia nigra and consists entirely of medullated axons of long conduction paths. Its middle third is occupied by the cerebrofugal pyramidal-tract fibers; medialward from these, lie the corticonuclear fibers for the nuclei of the motor cerebral nerves. Both sets of fibers come from the motor area of the cerebral cortex of the same side. The most medial portion of the pes is occupied by the frontal cerebrocortico-pontile path, and the most lateral portion by the temporo-occipital cerebrocortico-pontile path. These two paths, arising in the cerebral cortex (frontal, temporal, parietal and occipital) end in the nuclei pontis, whence other neuron systems extend the path to the opposite cerebellar hemisphere. Possibly, these bundles may carry paths running in both directions.

Most of these relations are diagrammatically illustrated in Fig. 587.

### (*a*) *Lesions of the Corpora quadrigemina*

The corpora quadrigemina are chiefly important for their optic and acoustic reflex functions through their connections, on the one hand, with the optic and cochlear paths, and, on the other, with the medial longitudinal bundle and the nuclei of origin of the motor nerves going to the eye-muscles. They control the movements of the eyes and the head under the guidance of optic and acoustic impulses.

In lesions of this part of the brain there may be:

1. Pupillary anomalies.

2. Unilateral or bilateral paralysis of the eye-muscle movements, either in the form of (i) total ophthalmoplegia externa and interna (with the exception of the M. rectus lateralis, innervated by N.VI), or of (ii) partial nuclear paralysis, in which single muscles, or groups of muscles, are picked out (*e. g.*, ptosis, partial or complete ophthalmoplegia interna, or partial ophthalmoplegia externa).

3. Nystagmus.

4. Visual disturbances due to lesion of the superior colliculi (more likely, to the adjacent optic tracts, or lateral geniculate bodies).

5. Deafness, not due to ear disease, but depending on bilateral involvement of the lateral lemnisci, or of the inferior colliculi (or, sometimes, the adjacent medial geniculate bodies in the interbrain).

6. Ataxia, or anesthesia, or both, due to pressure upon the underlying lemniscus medialis, or upon the red nucleus and brachium conjunctivum.

Here the disturbances of visual acuity, the eye-muscle paralyses, and the ataxia, when they occur, are probably due, not to lesions of the corpora quadrigemina themselves, but to associated involvement of the underlying tegmentum of the cerebral peduncle (neighborhood-symptoms). As far as the inferior colliculi *per se* are concerned, lesion on one side could cause slight impairment of hearing in both ears, and, especially, interference with the cochlear reflexes; similarly, lesions of the superior colliculi, in themselves, probably interfere only with the optic and oculomotor reflexes.

### (*b*) *Lesions of the Cerebral Peduncles*

The tegmentum and basis pedunculi may be simultaneously involved, in which case the lesions give rise to very characteristic syndromes. One of these is a complete hemiplegia of the side of the body opposite the lesion (face, tongue, arm, leg), combined with a paralysis of the oculomotor nerve on the side of the lesion (*hemiplegia alternans superior,* or *Weber-Gubler syndrome*). Sometimes the limbs of the paralyzed side show a marked tremor, usually of the type met with in paralysis agitans. The whole picture is then designated *Benedikt's syndrome.* The tremor is probably due to involvement of the tegmentum. It may be associated with hemi-ataxia.

Still a third variety of peduncular lesion occurs, that in which unilateral oculomotor paralysis is combined with cerebellar ataxia (*Nothnagel's syndrome*); here the lesion involves the oculomotor nuclei and the red-nucleus paths (brachium conjunctivum). When the ataxia is a movement-ataxia rather than a cerebellar ataxia, it points to a fourth type of lesion—involvement of the lemniscus rather than of the red-nucleus path; the syndrome is then further complicated by the presence of a crossed hemianesthesia.

Peduncular lesions can of course be due (1) to processes involving the peduncle directly, or (2) to basilar processes compressing it, or extending into it. If we remember the relation of the radix N. oculomotorii to the basis pedunculi we have the clue to hemiplegia alternans superior.

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[See also references on Hemiplegia alternans, p. 422.]

## 4. Lesions of the Interbrain (Diencephalon)

The interbrain, or diencephalon, includes (1) the region of the basal ganglia (nucleus caudatus, nucleus lentiformis, optic thalamus), (2) the internal capsule, (3) the central gray matter about the third ventricle,

(4) the hypothalamic region, (5) the epiphysis (or pineal gland), (6) the hypophysis (or pituitary body), (7) the corpora geniculata, and (8) the optic tracts and optic chiasm.

### (*a*) *Lesions of the Basal Ganglia*

#### i. The Corpus striatum

The functions of the *nucleus caudatus* and of the *nucleus lentiformis* (which, together, make up the gray matter of the corpus striatum) are but little known to us. Lesions limited to them, with the exceptions about to be mentioned, cause no symptoms that we recognize as yet, unless they extend to the neighboring capsule of white matter. The nucleus lentiformis includes the *globus pallidus* and the *putamen.*

In 1912, S. A. K. Wilson called attention to a syndrome that he has designated "progressive lenticular degeneration, a familial nervous disease associated with cirrhosis of the liver." The disease occurs in families but is not hereditary, comes on in early life, and is characterized by dysarthria, dysphagia, general tremor (most marked in the extremities), forced laughing and crying, sudden depressions of the lower jaw opening the mouth wide, muscular rigidity and contracture (though there are no signs of lesion of the pyramidal tracts), hypermimia, and slight enfeeblement of the intellect. The disease is fatal, progressing either rapidly (months) or slowly (4-7 years) to its termination. At autopsy, he found bilateral degeneration of the nuclei lentiformes, apparently toxic in its origin, and also cirrhosis of the liver, though symptoms referable to the liver were not observed during life. It seems probable, therefore, that paths run from the nucleus lentiformis through either the rubrospinal or thalamocortical system to exert an inhibitory influence upon the corticospinal paths.

In 1916, at the meeting of the American Neurological Association, J. Ramsay Hunt discussed the relations of the globus pallidus to paralysis agitans and to Huntington's chorea.

#### ii. The Thalamus

The *thalamus,* on the other hand, possesses several functions that we recognize.

In the first place, it is a way-station in the great centripetal (sensory) path. The axons of the sensory neurons of the second order that run through the lemniscus medialis terminate in the ventrolateral nuclei of the thalamus; in these nuclei are the cell bodies of thalamocortical neurons the axons of which run through the internal capsule to the somesthetic area of the cerebral cortex. Lesions, therefore, of this ventrolateral region of the thalamus may cause what has been described as the *thalamic syndrome* (Déjerine and Roussy) (1) contralateral hemianesthesia, especially bathyanesthesia, (2) violent and persistent pains on the anesthetic side, (3) sometimes a hyperesthesia especially on summation of stimuli, (4) hemiataxia, (5) hemichorea, or hemiathetosis, and (6) slight, temporary hemiparesis with hypotony and negative Babinski sign. Lesions further back may cause contralateral hemianesthesia of touch, pain, and temperature senses; one wonders, in the latter cases, whether or not the capsula interna has been involved in the lesion.

In the second place, the thalamus appears to be an important center for certain involuntary automatic movements, especially for the involuntary mimic and pantomimic expressive movements. The loss of mimic associated movements of the lower half of the face on laughing or crying, although these muscles of the face are still subject to voluntary control, is held to be a pathognomonic sign of lesion of the thalamus. On the other hand, when, in a hemiplegia, the involuntary mimic expressive movements are retained on the paralyzed side, we can, it is asserted, be sure that the thalamus and the thalamospinal paths have not been involved in the lesion. This dogma requires the control of exact clinical and pathological-anatomical studies. There is evidence that unilateral disturbance of the mimic expressive movements may follow a contralateral lesion of the cerebral cortex, without involvement of the thalamus.

In the third place, a portion of the optic tract ends in the pulvinar of the thalamus. Close to this lies the lateral geniculate body in which a majority of the fibers of the optic tract terminate. From the pulvinar and the lateral geniculate body arises the occipitothalamic radiation, which passes thence to the occipital cortex (central visual path). One understands readily, therefore, that lesions of the posterior third of the thalamus may cause bilateral homonymous hemianopsia (*q. v.*); when the latter is associated with symptoms of motor irritation (hemichorea, athetosis, hemiataxia) pointing to the thalamus, localization becomes relatively easy.

### (*b*) *Lesions of the Epiphysis, the Hypophysis cerebri, etc.*

The symptoms of involvement of the epiphysis cerebri, and of the hypophysis cerebri (or pituitary gland) are fully described in the chapter dealing with Diseases of the Endocrine Glands (*q. v.*).

Lesions of the *optic tract* and *chiasm* and of the *lateral geniculate body* will be considered along with other lesions of the visual conduction paths (*q. v.*). Lesions of the lateral lemniscus and of the *medial geniculate body* will be taken up when the cerebral auditory path is considered.

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## 2. *Lesions of the Thalamus*

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## 5. Lesions of the End Brain (Telencephalon), Causing Motor and Sensory Disturbances

The two *cerebral hemispheres* are united by the corpus callosum and by the commissures of the brain, and, below, are directly connected, through the basal ganglia, the internal capsule, and the cerebral peduncles, with the lower parts of the nervous system. Each cerebral hemisphere is covered over by a much-folded *gray cortex,* the different lobes being separated from one another by fissures, and the several gyri from one another by sulci.

The *white matter* consists of (1) association fibers connecting the different parts of one hemisphere with one another or with the other hemisphere and (2) projection fibers, which connect the cerebral cortex with the lower part of the central nervous system. The *projection fibers* include long tracts like the pyramidal tracts (corticofugal) and the various sensory conduction paths (corticopetal). The phenomena of consciousness and the activity of the "will" and of the "intelligence" (conative and cognitive functions) appear to be connected mainly, if not exclusively, with the cerebrum.

### (*a*) *The Motor Functions of the End Brain*

*(Motor Areas in the Cerebral Cortex, and the Centrifugal Paths Arising in Them)*

The motor area of the cerebral cortex (Fig. 588) corresponds in the main to the gyrus centralis anterior on the lateral surface and to a part of the lobulus paracentralis on the medial surface. Impulses arising here extend through the upper motor neurons to the nuclei of origin of the cerebral and spinal motor nerves, innervating chiefly the movements on the opposite side of the body and, to a less extent, those on the same side.

The representation in the cortex shows a distinct memberment, which agrees very well with the segmental arrangement of the reflex mechanisms in the spinal cord. The most lateral (inferior) part of the motor area controls the movements of the muscles of the face, the area next adjoining the muscles of the arm and of the trunk, while the most medial (uppermost) part of the area has to do with the movements of the leg and of the perineum; this last area passes over to the medial surface of the cerebral hemisphere. In addition to this continuous motor zone, there are at least two isolated areas of cortex in which the associated movements of the two eyes are represented; one of these lies near the tip of the frontal

lobe, the other lies at the tip, and, more especially, on the medial surface, of the occipital lobe (see Horsley's Linacre Lecture).

Movements originating in impulses that start in these motor areas of the cortex cause an ordered reciprocal innervation, certain "protagonist" muscles being excited simultaneously with inhibition of certain "antagonists," just as in the higher reflexes. It is interesting that the groupings of muscular contractions concerned in these movements, like the ordinary reflexes, have little, if anything, to do with the groupings of the muscles that are concerned in those static (or tonic) contractions that counteract gravity in the different positions that the body assumes. On the contrary, movements arising in the cortex seem to be concerned especially with the same muscular combinations as those that are met with in the

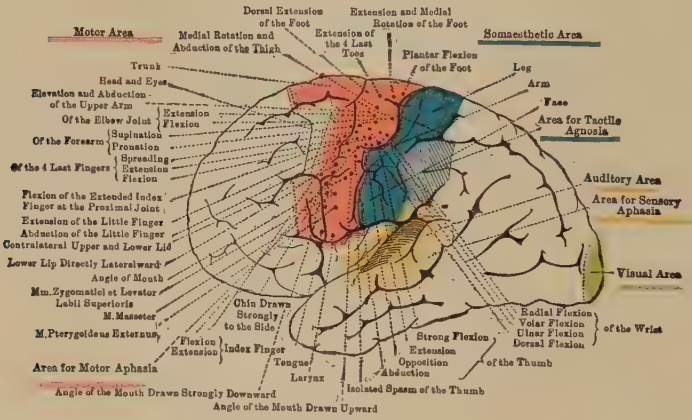


**Fig. 588.—The Localization of Function in the Cerebral Cortex. (After Kleist in Brugsch & Schittenhelm.)**

reflexes that defend the body from harmful influences, or are concerned in flight from such influences. They differ from these reflexes, however, in that they often assume the character of reactions to impressions received from the more highly specialized sense organs (touch, sight, hearing).

Mild electrical stimulation in the motor area of the cortex calls forth specific localized movements of the types mentioned. As the electrical current is strengthened, the movement spreads to adjacent parts of the body in the form of a *march;* this may last longer than the time of application of the stimulus and may go over into an epileptiform convulsion. Electrical stimulation of the axons of the upper motor neurons in the centrum semi-ovale, in the internal capsule, or in the pyramidal tract, calls forth movements similar to those that result from irritation of the cortex itself. They have the same ordered character, and, if the stimulation be strong enough, they take the form of epileptic convulsions.

Destruction of a portion of the motor area interferes with the movements represented there. In animals, the effects are very striking at first, but may vanish later, if the cortical injury has been slight. Though the pyramidal tract and the corticonuclear path to the cerebral nerve nuclei are the principal motor paths connecting the cortex with the lower motor neurons, there must exist other, probably less direct, paths to the spinal cord by way of the nucleus lentiformis, the nucleus ruber, and the formatio reticularis, for even after both pyramids are cut in animals, irritation of the motor areas still causes homolateral and heterolateral movements, though they are far less in extent than when the pyramidal tracts are intact.

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### (b) Lesions of the End Brain Causing Disturbances of Motility

The special regions in the motor area for the movements of the lower extremities, of the arm, face, tongue, for the movements concerned in speech, deglutition and mastication, as well as for the voluntary movements of the trunk and eyes, are illustrated in the accompanying figures.

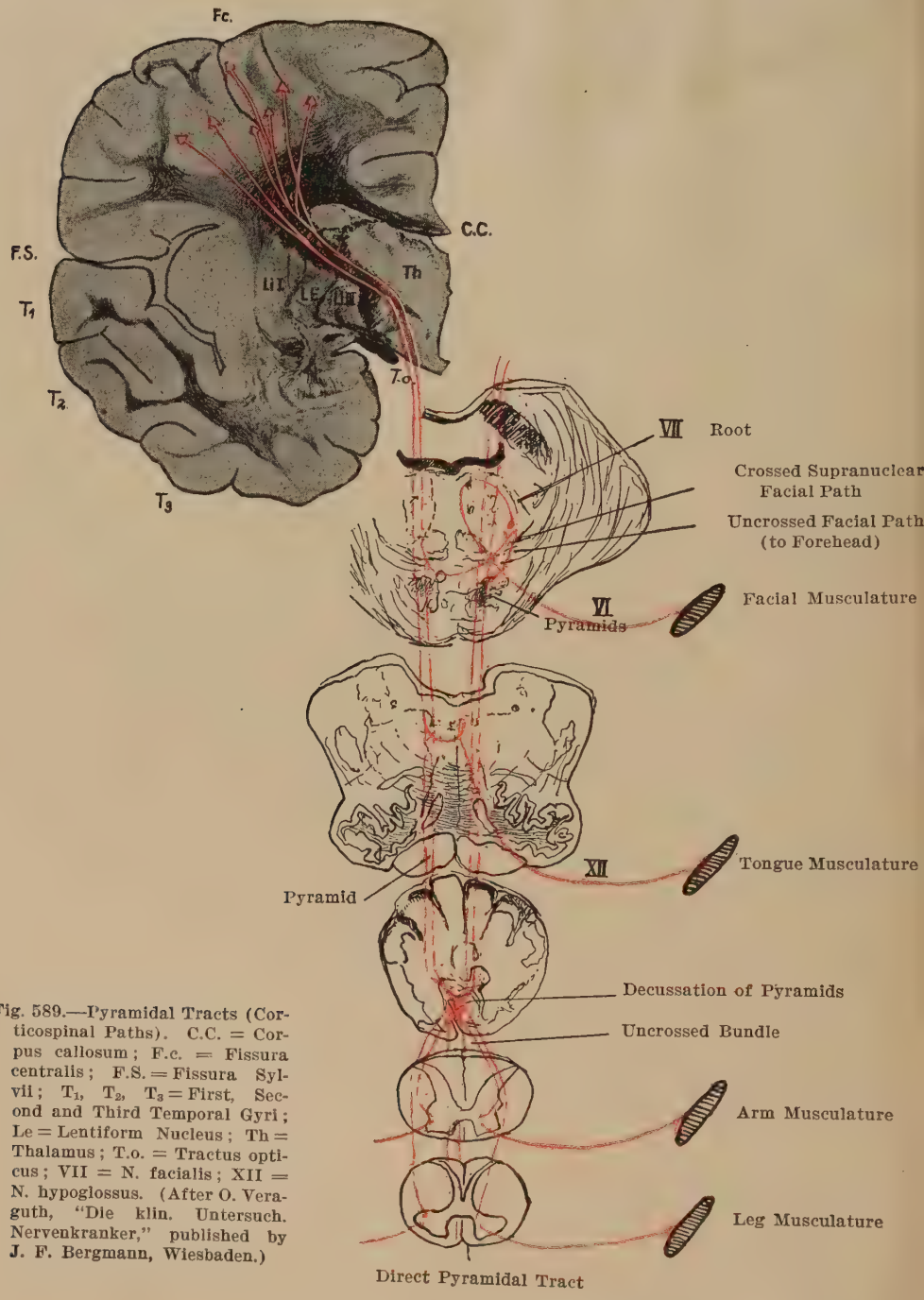


Fig. 589.—Pyramidal Tracts (Corticospinal Paths). C.C. = Corpus callosum; F.c. = Fissura centralis; F.S. = Fissura Sylvii; $T_1$, $T_2$, $T_3$ = First, Second and Third Temporal Gyri; Le = Lentiform Nucleus; Th = Thalamus; T.o. = Tractus opticus; VII = N. facialis; XII = N. hypoglossus. (After O. Veraguth, "Die klin. Untersuch. Nervenkranker," published by J. F. Bergmann, Wiesbaden.)

It should be remembered that many muscles, especially those of the "upper facial" domain, the jaw muscles, the muscles of deglutition, the laryngeal muscles, and the trunk muscles on each side, are represented in both cerebral hemispheres. A cerebral hemiplegia, therefore, due to a lesion in one hemisphere, causes only an incomplete paralysis of these bilaterally innervated muscles. Complete paralysis of movement in the muscle groups mentioned is observed in upper-motor-neuron lesions only in symmetrical lesions of both cerebral hemispheres, or when the cortico-nuclear conduction-paths of both sides have been destroyed; in lower-motor-neuron lesions, on the contrary, a unilateral lesion causes complete paralysis of movement in these muscle groups.

An application of this fact is made very often in the diagnosis of the cause of a facial paralysis. In both upper-motor-neuron lesion and lower-motor-neuron lesion the movements of the lower part of the face are paralyzed; but the upper-facial domain is only paretic in upper-motor-neuron lesion while it is totally paralyzed in lower-motor-neuron lesion.

### i. Lesions of the Motor Area of the Cortex

Owing to the relatively large surface over which movements are represented in the cerebral cortex, only a very large lesion (*e. g.*, thrombosis of the whole middle cerebral artery) could cause destruction of the whole motor area and a *complete hemiplegia.* Since smaller lesions are much more common in the cortex, focal lesions of the motor area more often give rise to *partial hemiplegias,* involving the arm alone, or the arm and face, or the arm and leg. Such *monoplegias* are accompanied by exaggerated reflexes and contracture, but there is no DeR in the muscles affected. Paralyses of this sort are frequently associated with disturbances of stereognostic perception, with localized bathyanesthesia (with no marked involvement of the senses of touch, pain and temperature), with slight symptoms of sensory irritation (local paresthesias), and, especially, with the particular form of motor irritation known as partial cortical epilepsy (*jacksonian epilepsy*), the convulsive movement beginning in the muscular domain corresponding to the site of the focal lesion, and extending in a definite march, corresponding to the anatomical arrangement of the cell-bodies in the upper motor neurons in the motor area, to the whole musculature of one half of the body, and sometimes passing over to the other side.

Occasionally, a localized lesion (gumma, encephalitis, tumor), giving rise, at first to monoplegia, or to jacksonian epilepsy, may gradually extend until it causes a complete hemiplegia; the origin and course of the affection are decisive for the diagnosis of the cortical situation of the lesion.

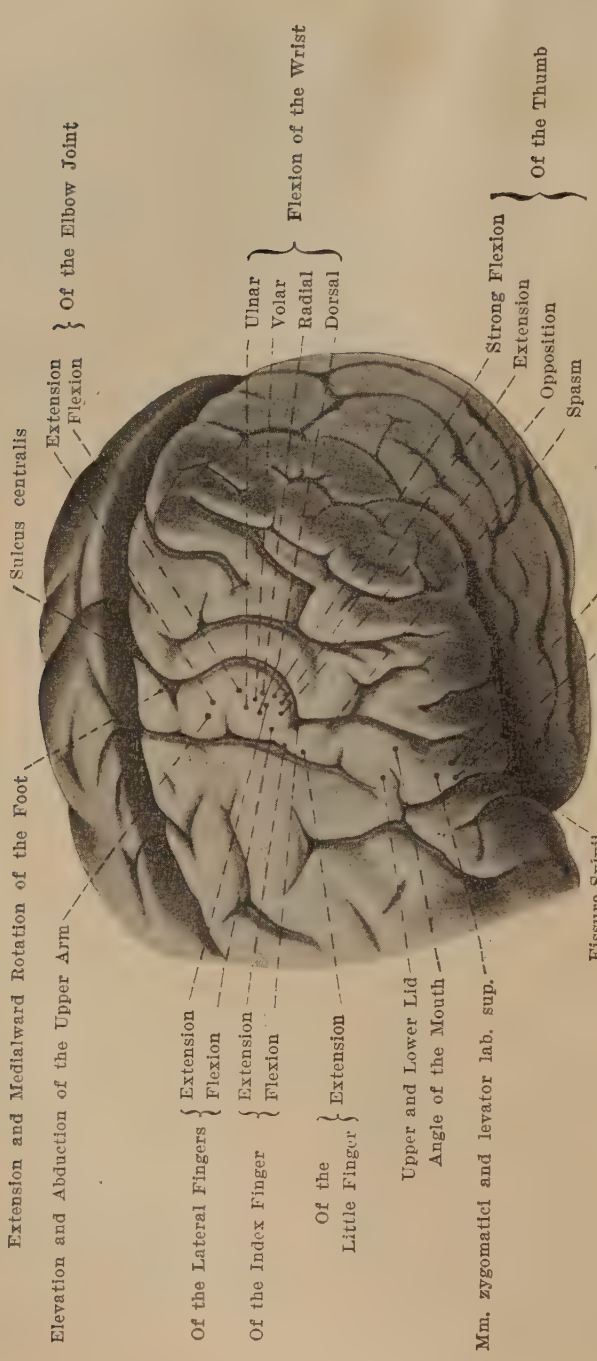


Fig. 590.—Left Hemisphere of Human Brain. Results of Faradic Stimulation at Operations. (After F. Krause in M. Rothmann's article in "Handb. d. inner. Med.," published by J. Springer, Berlin.)

### ii. Lesions of the Motor Projection Fibers in the Centrum semi-ovale

Lesions of the motor conduction path just beneath the cortex also give rise to monoplegias and to jacksonian epilepsy; it may, therefore, be impossible to say positively whether a small lesion is cortical, or immediately subcortical, in position. Owing to the fanlike convergence of the motor fibers as they run from the motor area of the cortex through the corona radiata of the centrum semi-ovale to the internal capsule, it is obvious that the farther below the cortex a lesion of given size is when it interrupts this motor path, the more likely it is to give rise to an extensive paralysis. Thus, immediately above the internal capsule, a hemiplegia would be caused by a lesion of a size that, near the cortex, would cause only a monoplegia. Again, the farther away from the cortex the lesion lies in the centrum semi-ovale, the less likely is the paralysis to be associated with symptoms of cortical irritation (sensory phenomena, jacksonian epilepsy).

### iii. Lesions of the Motor Fibers of the Internal Capsule

The *internal capsule* (capsula interna) is the site of the lesion in the majority of cases in which a hemiplegia is cerebral in origin. The motor path occupies the anterior two-thirds of the posterior (or occipital) limb of the internal capsule, that is, the white matter between the thalamus and the nucleus lentiformis; the fibers for the face, arm and leg lie so close together that even a very small lesion causes hemiplegia and not a monoplegia.

The fibers going to the nuclei of the facial and hypoglossal nerves lie farthest forward near the knee (genu) of the capsule; just behind them are the fibers for the movements of the arm, and still farther back those for the movements of the leg. In the posterior third of the posterior limb of the capsule lie the corticopetal fibers of the general sensory path; hence a lesion involving the whole posterior limb of the internal capsule causes not only a contralateral hemiplegia but also a contralateral hemianesthesia.

A *capsular hemiplegia* shows its cerebral origin in the slight participation of bilaterally innervated muscles (upper facial; muscles of mastication, deglutition and phonation; trunk muscles). One might not think the upper facial muscles affected at all unless he tested the strength of the M. orbicularis palpebrarum of the paralyzed side, when he would find that it cannot be so firmly contracted as on the healthy side. The movements in the lower facial domain are, however, markedly involved, as shown when the patient is asked to show his teeth or to retract the angles of the mouth. The tongue (being less powerfully innervated homolaterally) is deflected toward the paralyzed side when protruded.

Speech shows no disturbance as a result of unilateral interference with the corticobulbar path to the nuclei of N.VII and N.XII, except perhaps a slight, transitory, dysarthria, and there are no obvious disturbances in the movements depending on the other motor cerebral nerves, since they are all bilaterally innervated. The only disturbance of movements in

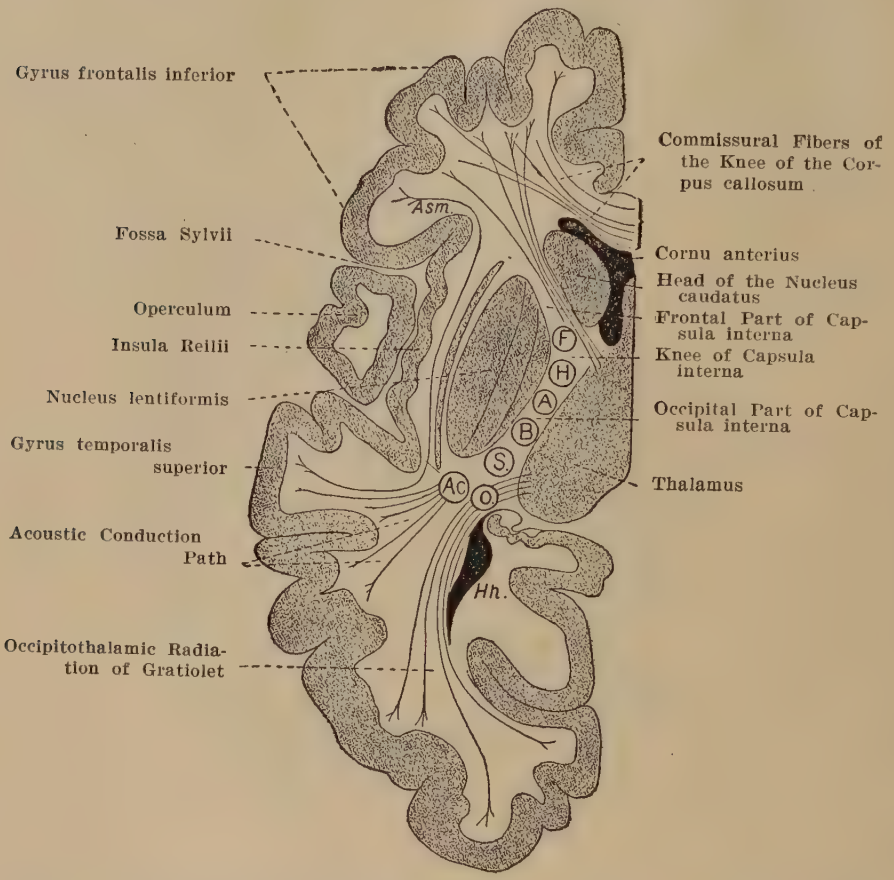


Fig. 591.—Horizontal Section of the Cerebral Hemisphere at the Level of the Pulvinar thalami optici. (Diagram After Monakow.) A, Motor Tract to the Arm; Ac, Acoustic Tract; Asm, Association Tracts Between Sensory and Motor Speech Centers; B, Motor Tract to the Leg; F, Motor Tract to the Face; H, Motor Tract to the Tongue; Hh, Posterior Horn of Lateral Ventricle; O, Optic Tract; S, Sensory Fibers.

the trunk are (a) slight lessening and a retardation of the expansion of the chest on the hemiplegic side on inspiration, and (b) some enfeeblement of the M. trapezius on that side. There is marked hypertony of the muscles on the paralyzed side (exaggerated reflexes, positive Babinski, later on, contractures). The paralysis is non-atrophic; there is no DeR, because it is the upper motor neurons, not the lower motor neurons, that

are involved, the only atrophy following being a slight wasting from disuse.

(The effects of lesions involving the motor path in the midbrain, medulla, pons and spinal cord have already been described.)

### (c) *Lesions of the End Brain Causing Disturbances of Common Sensibility and of the Special Senses*

Anatomical studies (Flechsig, Probst), physiological experiments (Munk, Horsley, Sherrington) and clinical-pathological observations (Mills, Keen, v. Monakow, F. v. Müller, Déjerine, Horsley, Spiller) make it seem probable that certain areas of the cerebral cortex (so-called "primordial sensory domains") are directly connected with the projection sensory paths that lead from the various sense-organs, whereas the rest of the cortex consists of so-called "intermediary and terminal domains" or "association-areas" (Flechsig), which are connected with one another and with the primordial sense areas and motor areas by means of association fibers.

These *primordial sense areas* are, therefore, the parts of the cerebral cortex first affected by impulses arriving in the cerebrum from the sense organs and from these must proceed impulses to the effector (motor) organs. All other parts of the cerebral cortex appear to be concerned with the working up of such excitations into higher complexes.

The sensory conduction paths of common sensibility, that is those mediating sensations of touch and muscle sense especially, and perhaps also those of temperature and pain, terminate in the so-called *somesthetic area* of the cerebral cortex (anterior and posterior central gyri, especially the latter; lobulus paracentralis; gyrus fornicatus). The fibers of the visual sensory path terminate in the *visual sense area* (pole and medial surface of the occipital lobe especially around the calcarine fissure). The auditory conduction path terminates in the *auditory sense area* of the cortex (island of Reil; adjoining parts of temporal and frontal lobes). The olfactory conduction path terminates in the *olfactory sense area* (uncus of the gyrus hippocampi). The position of the *gustatory sense area*, in which the taste fibers end is still uncertain, though it probably lies near the olfactory sense area.

The position of these primordial areas (motor regions and sense areas) and of the intermediary and terminal areas (association centers) are well shown in Fig. 588.

We have next to consider the effects of lesions injuring the primordial sense areas and the sensory projection paths in the cerebrum leading to them.

#### i. Lesions of the Somesthetic Area and its Corticopetal Projection Path

The somesthetic area, or primordial sensory domain, in the cerebral cortex, in which the fibers of common sensibility terminate, corresponds more or less closely to the so-called motor area of the cortex, though there is this difference, that the cell-bodies of the upper motor neurons are predominantly located in the anterior part of the area (gyrus centralis anterior, lobulus paracentralis), while the sensory path terminates predominantly in the posterior part of the area (gyrus centralis posterior, lobulus parietalis). A lesion in the somesthetic area, causing disturb-

ances of sensation, is, accordingly, since it so closely adjoins, or overlaps, the motor area, usually accompanied by paralysis, or by symptoms of motor irritation. Small lesions in the somesthetic area of the cortex itself, or of the white matter of the corona radiata of the centrum semiovale near it, give rise to *mono-anesthesias* or to *mono-paresthesias* in very limited domains (thumb, finger, hand, etc.). Moreover, the sensory disturbances in such cases are prone to consist especially of disturbances of the power of localization of tactile stimuli, of deep sensibility (bathyanesthesia), or of stereognostic perception.

Lesions of the somesthetic projection path lower down (internal capsule, hypothalamic region, lemniscus medialis in its course from the medulla oblongata through the tegmentum of the pons and the cerebral peduncle) cause loss (or impairment) of common sensibility of the opposite half of the body, this somanesthesia being usually associated with hemi-ataxia of the corresponding extremities. As we have already seen, lesions of this somesthetic projection path in the pons, or in the medulla oblongata, may give rise to a so-called *hemianesthesia cruciata*, that is, to an anesthesia of the face on one side of the body, and of the arm, trunk and leg of the other side of the body; the exact position of such a lesion is often localizable by a consideration of the accompanying symptoms referable to cerebral nerves other than the N. trigeminus.

Though injury to the somesthetic projection path, or the somesthetic area, alone, interferes with common sensibility only, there is one situation in which lesions destroying the somesthetic conduction paths are prone to destroy also the projection paths for the higher sense organs (visual, auditory, gustatory), thus causing a *total contralateral hemianesthesia* (general cutaneous anesthesia and bathyanesthesia, combined with bilateral homonymous hemi-anopsia, partial deafness and ageusia). We refer to focal lesions causing destruction of the posterior part of the posterior limb of the internal capsule (*carrefour sensitif* of Charcot). When such lesions extend forward, so as to involve also the anterior part of the posterior limb of the capsule and its knee, the total hemi-anesthesia is accompanied by a hemiplegia.

**Symptoms of Somesthetic Irritation in Telencephalic Lesions.**—Paresthesias, and pains, located in one extremity, or in one half of the body, if due to an irritative lesion of the sensory-motor area of the cortex, are usually accompanied either with paralysis, or paresis, of the corresponding portion of the body. Jacksonian epilepsy is not infrequently preceded by a somesthetic aura. Occasionally, pains in the opposite half of the body result from subcortical or from diencephalic lesions (see Thalamic Syndrome of Roussy, already described); they may be the only signs of an apoplexy.

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### ii. Lesions of the Visual Sense Area and of its Corticopetal Projection Path

The visual conduction path from the retina, through the optic nerves, chiasm, optic tracts, lateral geniculate body, pulvinar and the occipito-thalamic radiations to the cuneus has already been referred to.

**Unilateral Lesions.**—Lesion of one visual sense area (cortex about the calcarine fissure), or lesion of the visual conduction path of one side posterior to the optic chiasm, causes *homonymous bilateral hemi-anopsia.* Thus a focal disease on the left side causes blindness in the right visual field of both eyes (*hemi-anopsia bilateralis dextra*), while a similar lesion of the visual conduction path on the right side of the brain leads to loss of the visual field on the left in both eyes (*hemi-anopsia bilateralis sinistra*). Such a bilateral homonymous hemi-anopsia, of itself, tells us only that the lesion is situated somewhere between the optic chiasm and the visual sense area in the occipital lobe of one side. For exact localization,

we must rely upon certain accompanying symptoms. Thus, if the lesion involve the tractus opticus, it is prone to involve simultaneously the roots of the cerebral nerves at the base of the brain. Or, the optic tract may be compressed by a tumor, or abscess in the overlying temporal lobe, in which event, the hemi-anopsia may be associated with aphasia and with olfactory hallucinations.

Lesions in the visual conduction path situated in the region of the primary optic centers, that is, at the point where the optic tract ends in the lateral geniculate body and the pulvinar of the thalamus, whence the occipitothalamic radiation sets out, often causes a hemi-anopsia that is part of a total hemi-anesthesia (with or without hemiplegia) from simultaneous involvement of the structures of the adjacent internal capsule. The hemi-anopsia due to lesion of the visual sense area in the cortex may have no accompanying motor, or other sensory, anomaly.

The so-called hemi-anopic pupillary reaction of Wernicke for distinguishing hemi-anopsias due to lesions between the optic chiasm and the geniculate body, on the one hand, from those arising from lesions between the geniculate body and the occipital lobe, on the other, was, as has already been pointed out, based on a faulty idea regarding the distribution of the pupillary fibers in the retina (see The Pupillary Reactions).

**Bilateral Lesions.**—Bilateral lesions involving both visual sense areas in the cortex, or both occipitothalamic radiations, or the region of the primary optic centers (lateral geniculate body, pulvinar) on both sides, can cause a *double bilateral homonymous hemi-anopsia* with retention of central vision, or, in some instances, *total blindness.*

### *Lesions of the Chiasma opticum*

In lesions of the optic chiasm (especially from enlargement of the hypophysis), there may be a loss of the temporal half of the visual field on both sides (*hemi-anopsia bitemporalis*). It is obvious that a lesion that can involve the lateral uncrossed fiber bundles of the chiasm on both sides, causing a loss of the nasal half of the visual field of both sides (*hemi-anopsia binasalis*) and leaving the crossed fibers intact, must be very rare; it does, however, sometimes occur.

**Disturbances of Vision Limited to One Eye.**—Visual disturbances limited to one eye do not arise from lesions behind the chiasm; they point, therefore, to lesions either of the optic nerve, or of the retina (see The Visual Sense and its Disturbances).

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### iii. Lesions of the Auditory Sense Area and of Its Corticopetal Projection Path

Lesions of the auditory sense area on one side, only, give rise to temporary and partial deafness, owing to the fact that the auditory paths have undergone partial crossing lower down (corpus trapezoideum). Bilateral affections may, however, cause complete deafness.

The same statement is true of the auditory conduction path extending from the pons through the lateral lemniscus, medial geniculate body and internal capsule, to the auditory sense area in the temporal lobe.

Irritative lesions of the auditory sense area, or of the auditory conduc-

tion path, are, probably, the cause of auditory hallucinations (akoasmata, voices), though it may be that higher associative areas are the seat of the irritation.

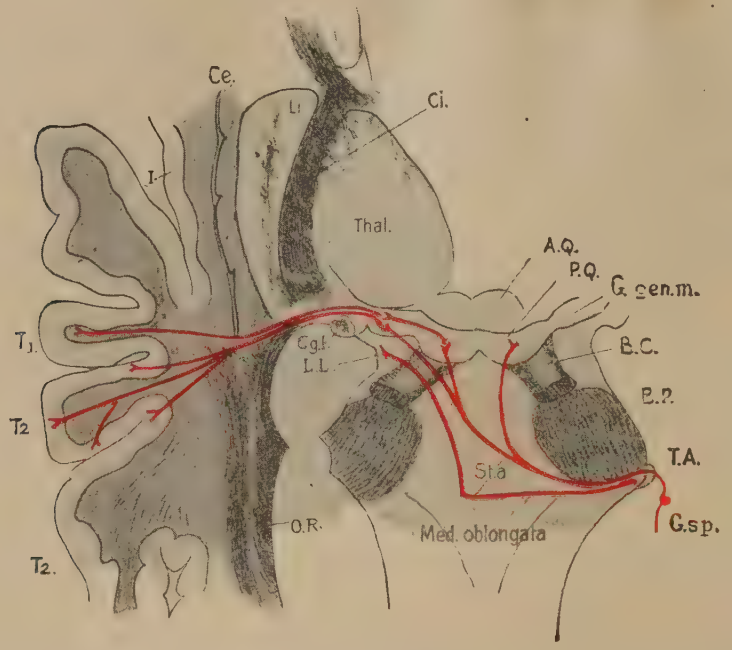


Fig. 592.—Diagram of Central Paths of N. cochlearis. $T_1$ and $T_2$ = First and Second Temporal gyri; I = Island; Ce = Claustrum; Li = Lentiform Nucleus; Ci = Internal capsule; Thal. = Thalamus; L.L. = Lateral lemniscus; O.R. = Optic Radiation; A.Q. = Ant. corp. quadrigemina; P.Q. = Post corp. quadrigemina; B.C. = Brachium conjunct.; B.P. = Brachium pontis; C. gen. med. = Medial Geniculate Body; C.g.l. = Lateral Geniculate Body; St.a. = Striae acusticae; G.sp. = Ganglion spirale; T.A. = Tuberculum acusticum. (After v. Monakow in O. Veraguth's "Die klin. Untersuch. Nervenkranker," published by J. F. Bergmann, Wiesbaden.)

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### iv. Lesions of the Olfactory and Gustatory Sense Areas and of Their Corticopetal Projection Paths

Irritation of the uncus may cause olfactory hallucinations; destruction of this area, on one, or on both sides, may cause unilateral, or bi-

lateral, anosmia. Some observations indicate that lesions of the anterior part of the gyrus fornicatus cause disturbances of taste. Tumors involving the uncus, giving rise to the *uncinate gyrus fits* of Hughlings Jackson, with olfactory and gustatory hallucinations, smacking of the lips, and movements of the tongue, point (1) to a close proximity of the olfactory and gustatory sense areas, and (2) to a special motor area in the same neighobrhood for the lip and tongue muscles.

Lesions of the bulbus olfactorius, of the lobus olfactorius, or of the trigonum olfactorium may cause anosmia.

The cortical representations of hunger and thirst sensations are still unknown; it has been suggested that they lie on the basal surface of the temporal lobe. We are in ignorance, also, of the cortical representation of the libido sexualis, and of the sexual orgasm.

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## 6. Lesions of the End-Brain (Telencephalon) Involving the Higher Association-Centers or the Paths Connecting Them

*(Topical Diagnosis of the Aphasic, the Agnostic and the Apraxic Disturbances)*

Each primordial area in the cortex (motor and sensory) is connected (1) by short association paths, with areas of the cortex near by, and (2) by long association paths, with more distant areas in the cerebral hemisphere of the same side, and (3) through the corpus callosum and commissures, with areas of the opposite side.

The functions of these higher associative neuron systems of the cerebral cortex are very complex, but psychological clinical observations, in combination with pathological-anatomical studies, are beginning to throw

some light upon the manner in which the activities of the sense areas are combined with one another and worked up to higher units; we begin, through such studies, to get clues as to the parts of the brain concerned in this higher work. Here belong the data collected regarding (1) the disturbances of the power of speaking ourselves, of understanding the speech of others, of writing, and of reading—the so-called aphasic disturbances; (2) the disturbances of the power of identification—the agnosias, and (3) the disturbances of the non-symbolic movements—the apraxias and dyspraxias. The general symptomatology of these conditions has already been described; we shall now turn to a consideration of the facts bearing upon the localization in the end-brain of the lesions that give rise to them.

Very great difficulties are sometimes experienced in distinguishing the various forms of agnosia, aphasia and apraxia that have been described, and the young physician should not be discouraged, if in his early attempts, before he has attained to skill in psychological analysis, he be somewhat perplexed; even the most experienced observer will sometimes be in doubt.

The topical diagnosis of these disturbances is, as yet, far from satisfactory, though since the early investigations of Broca (1861) on motor aphasia and of Wernicke (1874) on sensory aphasia, considerable progress has been made. As yet, however, we can speak positively regarding the very rough localization of only the more outspoken of these processes. The finer localization, and, especially, the differences in localization for the different clinical subforms of these disturbances, remains yet to be worked out.

For a full account of the present status of knowledge in this domain the collective reviews of Heilbronner, Wyllie, von Monakow, Moutier and Quensel, should be consulted. Only the better-established facts will be referred to in our brief review.

### (*a*) *Distribution of Functions Between the Two Cerebral Hemispheres*

Since Broca's time, the predominance of lesions of the left hemisphere in aphasic disturbances has been known. In left-handed people, however, the right hemisphere takes the place of the left. In both cases, however, the less dominant hemisphere may also be concerned in aphasic, apraxic, and agnostic disturbances. Thus temporary motor aphasia is occasionally met with in left-sided hemiplegias (lesions in right hemisphere), even in right-handed people. Foster Kennedy lays stress upon a study of the ancestry for left-handedness in such people.

For the apraxic disturbances, lesions of the left hemisphere are also more important than those of the right, though the dominance of the left hemisphere is not so marked as in the aphasic disturbances. It seems

certain that there is a center in the left hemisphere that represents the praxic movements of the extremities of both sides, or, at any rate, when injured, it can cause apraxia or dyspraxia on both sides.

The functions of the two hemispheres seem to be more equal as regards the power of secondary identification, as indicated by the results of the lesions that cause agnostic disturbances, though a certain preponderance of the left hemisphere can here also be made out.

## (*b*) *The Mechanisms of Speech*

### i. Memories of Word-sounds

When a child learns to speak, it stores up memories of the sounds of words heard, in an area adjacent to the auditory sense area; this contains the neuron systems for word-sound memories, the so-called *sensory speech center*. At first, the brain attends especially to the rhythm, clang-color, and pitch of sounds; later, it learns to distinguish, in the melody of speech, the individual words, and to associate the word-sounds with their meaning (a complex of associated memory-pictures). When a familiar word is heard by the child, the "memory-pictures" are awakened, and the child recognizes the word, and, as we say, understands it. On this receptive side, too, the sensations of the muscular contractions during movements of the lips and tongue play a part; later (see Reading), optic impressions become associated with those of hearing and of muscle sense. The constant association of certain ideas with words, heard and seen, leads to the *use of words as symbols for ideas* in intercourse with the external world. The growth of ideas is greater and quicker than the growth of the child's vocabulary.

When the child begins to produce speech, that is to talk, he first utilizes the expressive movements (cooing, laughing, crying), then begins to be able to make articulate expression with the buccal, laryngeal, and respiratory muscles. His earliest articulate sound-productions are associated with vague feelings of pleasure or displeasure; next he makes the sounds "ma-ma" when any woman is near him, then learns to identify the sound "ma-ma" with one person, his own mother; only later on does "ma-ma" come to connote its fuller meaning and relationships. In making the delicately coördinated speech movements (glottis, palate, tongue, lips), he utilizes the memories of the sounds of words deposited in his sensory speech center in the temporal lobe.

### ii. Memories of the Innervations of the Speech Movements

By virtue of the constant attempts at repetition of words heard, through movements of his speech muscles, the child gradually collects memories of the innervations of the speech movements in a set of neurons located in a cortical area known as the "center for motor speech memories." This area is supposed to be, in right-handed persons, the foot of the third left frontal convolution (Broca's area), which, accordingly, has been designated the *motor speech center;* in it, the suprapyramidal innervations for the excitation of the pyramidal system governing the muscles of speech are supposed to originate. In other words, it is believed that the motor speech center contains the cell-bodies of neurons that send axons to terminate upon the cell-bodies of the upper motor neurons in the general motor area in the region in which movements of the tongue, lips, and larynx are represented.

Obviously, the sensory speech center must be connected with the motor speech center by conduction paths, and, in our early attempts at talking, the speech movements are, it is believed, performed under the constant control of this sensory center for the memory of word-sounds. It seems probable that, later on in life, the motor speech center may attain to a degree of independence so great that, when an idea arises in consciousness, the ideas for the speech movements of the corresponding words can arise at once in the motor speech center without, necessarily, a preliminary revival in the sensory speech center for the memory of the sounds of the words, that is to say, the speech movements can be started by impulses sent directly from the higher areas through the "motor speech center" to the motor area in the anterior central gyrus without preliminary voyage over the sensory center for speech sounds. All through life, however, when we are thinking, or when we are looking for a word in our minds, it is common to hunt first for the memory of the sound of the word and to trust it to awaken our memory of the innervations of the muscles necessary for pronouncing it.

### iii. The Higher Mental Processes and the Speech Centers

It is believed that by means of association neurons all the sense areas in the cerebral cortex are connected both with the sensory speech area (for the memory of word-sounds) and the motor speech area (for the memory of the innervations of the movements necessary for producing words). Since words are symbols, which we use for designating concrete objects, or for expressing relations between these, the necessity of a connection of the areas of the cortex, in which memories of the various sense perceptions are stored, with the speech areas, is obvious. Every conception (or idea) of a concrete object is made up of a number of constituents; it may be regarded as a sum of memory-pictures of an associated group of different sense perceptions. Let us take an example. Our idea of a dog is made up of optic, acoustic, tactile, and olfactory memory-pictures. We have seen dogs, heard them bark, felt of them, and smelled them. Memories of these various sense perceptions are stored up, as we have seen, in different parts of the cerebral cortex. Now the sound of the word "dog," or the tendency to pronounce the word "dog," may be set up by optic memories, acoustic memories, tactile memories or olfactory memories, indeed, by any one of the partial memories of which the whole idea "dog" is composed. Normal speech depends upon the integrity, therefore, not only of the sensory and motor speech centers, and of the path connecting the motor center with the speech muscles, but also of the paths connecting the various sense areas of the cortex (or, rather, "identification areas") with the speech centers. Interruption of any one of these paths may disturb the normal process of transformation of conceptions into words.

## (c) *The Wernicke-Lichtheim Schemata*

The classification of the disturbances of speech known as the aphasias, usually adopted, is that of Wernicke, or some modification of it (Lichtheim's). Such classifications are largely theoretical and make use of schemata, which probably have some didactic value; but they should be regarded as mere schemata, if used at all; the tendency of the recent writers on aphasia is to abolish the aphasia-diagrams, and the aphasia-schemata. To understand the historical development of the subject, however, and to get a grasp of the technical terms already in use, some reference to these diagrams and schemata must be made. The diagrams are really useful if we bear in mind (1) that they are merely schemata, and (2) that the

lines and circles composing them do not represent compact bundles of nerve fibers or sharply circumscribed cortical areas, but rather are symbolic of the psychophysiological elements of which speech is a compound.

Wernicke divided the aphasias into two great classes: (1) motor aphasia, and (2) sensory aphasia. By *motor aphasia,* he meant loss of the power to produce speech, that is the loss of the power to revive in consciousness the memories required for innervating the word-movements, though the understanding of speech heard is retained, or only slightly disturbed. By *sensory aphasia,* he meant inability to understand speech heard; that is, though the patient hears words spoken, he does not understand what is said, since he has lost the capacity for reviving these memories of word-sounds, through which he recognizes words and understands their significance. In spite of this loss of the understanding of spoken words, he can himself speak, though his own speech will be more or less imperfect according as he has relied more or less upon the revival of word-sound memories for awakening and serially arranging the innervations of the movements made in speaking.

In the scheme (Fig. 593), therefore, motor aphasia could be due to a lesion of Broca's motor speech center at (B), and sensory aphasia to a lesion of Wernicke's sensory speech center at (W), but obviously disturbances could arise either from lesions of the centers themselves, or from lesions involving the paths going to or from these centers. Accordingly, Wernicke spoke of the symptoms due to lesions of the cortical centers (B) and (W) as *cortical aphasias;* of the symptoms due to lesions interfering with the association fibers connecting the portions of the cortex (I) concerned in the formation of conceptions with (B) and (W), that is, anywhere along the lines (B-I) and (W-I), as *transcortical asphasias;* of the symptoms due to lesion of the association paths connecting the motor speech center with the motor area of the cortex where the corticonuclear paths for the speech movements begin along the line (B-M), or connecting the sensory speech center with the auditory sense areas of cortex upon which it depends along the line (W-A), as *subcortical aphasias,* motor and sensory; and, finally, of the symptoms due to lesions interrupting the path connecting Wernicke's sensory speech center with Broca's motor speech center along the line (W-B) as *conduction aphasia.*

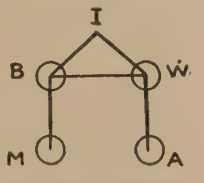

Fig. 593.—Diagram Illustrating the Simpler Disturbances of Speech.

**Reading.**—In *alexia,* inability to read, a distinction is made between (1) ability to understand printed or written words seen, and (2) ability to read aloud. The memory traces for the signs used in printing and writing (*i. e.,* the letters) are probably located in the periphery of both visual sense areas. Most people on reading have to revive in memory also the corresponding sounds of words. A child, in learning to read, reads aloud at first, always associating the optic impressions of the letters with their sounds and with the kinesthetic impressions of the corresponding speech movements. For instance, in combining the letters d, o, g into "dog," the child associates always the optic, the auditory, and the kinesthetic components; ever after on seeing the word "dog," he revives the sound in consciousness, and the perception is a combination of visual sensations with visual, auditory, and kinesthetic memories. Many people, on reading, also make the corresponding speech movements (either aloud or to themselves). This is why injuries in the domain either of the sensory or of the motor speech centers can also cause alexia. In graphically representing the conditions underlying reading and writing, Fig. 594 is usually employed. Conduction paths pass from the area of visual memories (O in the scheme) to the other centers, through the path leading to Wernicke's sensory speech center; the cortical area for the memories of word-sounds, (W)

is used in reading, either as O-W-I, or, on reading aloud, as O-W-I-B. Many people probably have a direct path from O-M; such persons transform the visual directly into movement innervation pictures, and first understand what they read when they speak it, using the path O-B-I, or perhaps O-B-W-I, simultaneously reviving word-movement memories and word-sound memories in consciousness. In artists, or in other persons in whom the visual power is markedly developed, there may be a direct path O-I.

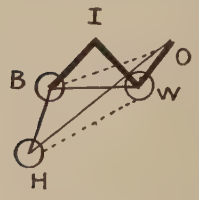


Fig. 594.—Diagram Illustrating Disturbances of Speech, Reading, and Writing.

Alexia is more commonly an accompaniment of sensory aphasia than of motor aphasia, though it may occur in either. Alexia may also occur as an isolated symptom—so-called *pure alexia.*

**Writing.**—There must, it is thought, be a direct path (O-H) from O to the motor center in the cortex for the right hand, which is used in copying (without understanding what is written). In spontaneous writing, the path I-W-O-H is probably used; the memory of the sound of the word is first revived, then the visual memory of the signs of writing, after which the motor center (H) is called into activity. Whether (H) is identical with the pyramidal tract beginning, or represents a suprapyramidal cortical area like (B), has been much discussed. In writing to dictation, the path W-O-H or W-O-B-H would be followed.

*Agraphia,* or inability to write, is sometimes associated with motor aphasia, even in cases in which the right hand is not paralyzed. It is not, however, a necessary accompaniment of motor aphasia; the power of writing is to a certain extent, in some persons, at any rate, independent of the power of speech.

Agraphia is more frequently present in sensory than in motor aphasia, probably because most people must revive word-sound memories before they can re-awaken the visual memories of written words prerequisite for the motor impulses for the production of writing. Patients that cannot write spontaneously may, however, be able to copy slavishly what they do not understand, an indication, it has been thought, of the existence of a direct path from the visual areas to the motor center for the right hand (O-H). An *isolated agraphia* (with retention of speech and the understanding of speech) is very rare (*q. v.*).

It does not seem probable that many people possess an especial center in which the memory of the movements requisite for the production of writing signs is located. People, however, who are able to write directly with the help of optic memory-pictures might have an isolated agraphia from interruption of the conduction paths connecting the optic memory with the left motor center (*e. g.,* tumor in the parietal lobe). If one assume that writing is always preceded by internal speech, then an isolated agraphia could result from interruption of the path from the motor speech center (B) to the motor center for the right hand (H). In most people, the power to write depends upon the integrity of the word-sound memory center and the paths connecting it with the motor center of the hand.

From what has been said, it will be clear that the power slavishly to copy from a sample is retained in all varieties of aphasia; that the capacity to write to dictation (without understanding) is lost in all forms of aphasia except (a) the transcortical aphasias and (b) the subcortical motor aphasia; and that spontaneous (understood) writing is intact only in the subcortical forms of aphasia, for in all other forms it is either entirely impossible, or if possible at all, paragraphic.

**Optic and Tactile Aphasia.**—In rare instances, patients see and recognize objects held before them but are unable to call them by name, although they otherwise speak naturally and, furthermore, are able to find the name of the object by the use of other sense organs.

For example, a patient suffering from *optic aphasia*, looking at a pocket-handkerchief, though knowing that it is used for wiping the nose, may be unable to give the name until he takes it in his hand. He seems unable to use his visual memories for speech. The symptom occurs in connection with lesions lying at the junction of the left occipital with the left temporal lobe, but the lesions must be extensive enough, apparently, to cut off the conduction paths connecting the occipital lobes of both sides with the temporal lobe on the left side. The disturbance is, therefore, usually associated with alexia and hemianopsia, and, sometimes, with sensory aphasia.

A similar *tactile aphasia* occurs occasionally. Though the patient is capable of tactile sensation, and identifies the object, he cannot give the name of the object felt. This differs from the tactile agnosia (already described) in that, in the latter, the patient does not recognize what he feels. In tactile aphasia he may recognize the object, but be unable to name it.

It is not improbable that olfactory and gustatory types similar to these optic and tactile types of aphasia will ultimately be recorded.

### (*d*) *The Aphasic Syndromes Actually Met with Clinically*

Under methods of examination we have dealt with the elementary disturbances of speech (1) on the expressive and (2) on the receptive side. Here the types of cases met with clinically, in which aphasic disturbances occur, must be outlined. Aside from all schemata, and proceeding objectively, we divide the aphasic syndromes into two great groups: (1) the simpler forms, and (2) the complex forms.

In the *simpler forms of aphasia* the clinical picture is limited to a single symptom, or to a few symptoms that must logically depend on one another, as, for example, the loss of the power of repetition depends on the loss of understanding of the speech-sounds.

In the *complex forms of aphasia* there are a series of symptoms not necessarily reciprocally interdependent; these complex syndromes include the majority of the aphasic cases met with in practice. While no two cases showing a complex form of aphasia are identical, still the complex forms can be arranged in groups so that they can nearly all be included, roughly at least, under a few types. In making this arrangement we depend chiefly upon the behavior of the patient (1) as regards the power to produce speech (motor speech), and (2) as regards the power of understanding speech. As a rule the behavior as regards reading and writing is not necessary for the placing of a case in a given group; this is fortunate, since the disturbances of reading and writing are very inconstant. An exception to this rule occurs in the differentiation of pure word-dumbness from Broca's aphasia (*q. v.*).

#### i. The Simpler Forms of Aphasia

Under this heading we shall consider (1) pure word-dumbness, (2) pure speech-deafness (or word-deafness), (3) pure agraphia, (4) pure alexia.

### (*1*) *Pure Word-Dumbness* (*Subcortical Motor Aphasia of Wernicke; Pure Motor Aphasia of Déjerine*)

Clinically, this is easy to recognize, since the disturbance of speech is restricted to the loss of power to speak, and this loss is usually complete and permanent, except for the slight "recurring utterances" of Hughlings Jackson. The patients know the words that they wish to say, but cannot remember how to innervate the speech movements necessary to produce the sounds of the words; by pressure of the hand, or by gestures, they can, however, often indicate the number of syllables in the word they desire to pronounce (Lichtheim's test).

This pure word-dumbness can be differentiated from Broca's aphasia by the fact that reading and writing are not at all disturbed.

Right-sided hemiplegia, or paresis of the face and tongue on the right side, are common, but not constant, accompaniments. Pure word-dumbness may appear, as such, immediately after the cerebral insult; sometimes there is a Broca's aphasia first, and, later on, as partial restitution occurs, a pure, or almost pure, word-dumbness remains.

### (*2*) *Pure Speech-Deafness* (*or Word-deafness*) (*Subcortical Aphasia of Wernicke; Pure Word-deafness of Déjerine*)

The clinical diagnosis of this condition requires great care; many of the cases reported as such in the bibliography do not belong in this group.

The condition is characterized by (1) loss of understanding of the sounds of words and of the sense of words, and (2) loss of the power of repetition. All other speech-functions on the expressive side are retained; and reading and writing are undisturbed in the typical cases.

One must first make sure that the loss of understanding of speech is not due to labyrinthine deafness, or to deafness due to bilateral cerebral lesions. Here a thorough otological investigation is necessary. Occasionally a case is met with in which there is pure speech-deafness in addition to labyrinthine deafness.

In most cases the power to understand speech is complete, and extends even to the identification of the speech-sounds as such; in a few cases, however, the sounds of the single letters can be understood, so that cases of "partial pure speech-deafness" have to be admitted.

In some of the cases of pure speech-deafness, sounds other than those of speech can be understood, but, in other cases, mind-deafness (auditory agnosia) is associated with the word-deafness.

As a rule pure speech-deafness is a persistent condition. Like pure word-dumbness, it sometimes occurs as the sole effect of a cerebral lesion; sometimes it remains as a residue after partial recovery from a Wernicke's aphasia.

### (3) *Pure Agraphia (Isolated Agraphia of Wernicke; Pure Motor Agraphia of Pitres and of Déjerine)*

Under this heading are included only the cases in which there is disturbance of writing independent of any other disturbance of speech-production, or of the understanding of speech. We exclude, especially, cases in which there is any involvement of reading, and of the complex known as the "letter-word" or "literal word." We exclude, also, the cases in which writing with the right hand only is impaired owing to paresis or ataxia. Cases of pure agraphia, despite sufficient motility of the right hand, have long been known; recently the existence of a bilateral agraphia without other aphasic disturbances has been demonstrated. The latter is, in some cases, an "apraxic agraphia."

### (4) *Pure Alexia (Subcortical Alexia of Wernicke; Pure Word-blindness of Déjerine; Isolated Alexia of Heilbronner)*

In this condition, only the power to read is lost. In typical cases the disability is so great that individual letters cannot be recognized, though figures, and sometimes the patient's own name, can be recognized and read. In less severe cases single letters can sometimes be recognized, though this slight power is quickly lost during the examination, owing to fatigue. Some patients can recognize and pronounce the letters that they write themselves from a copy, but some patients do not know that the signs are letters at all; they are unable to distinguish letters from other figures, in which event there may coexist an optic agnosia (mind-blindness).

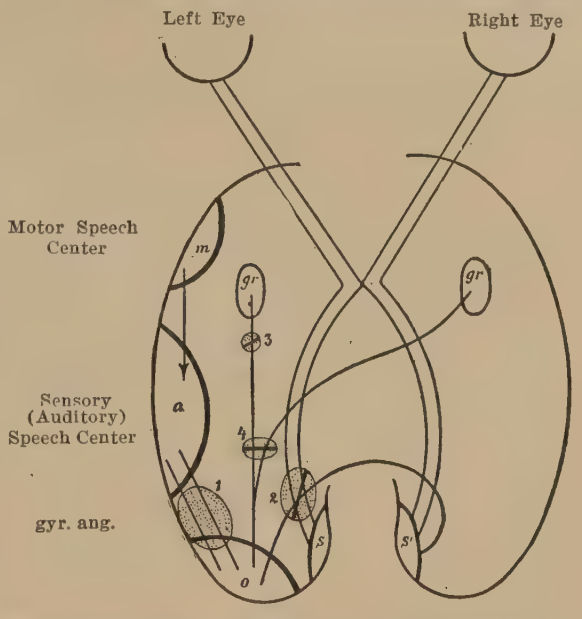


Fig. 595.—Diagram of Alexia and Agraphia. (After Liepmann.) Lesion 1 = Alexia and Agraphia; Lesion 2 = Pure Alexia with Hemi-anopsia; Lesion 3 = Pure Agraphia, of Right Hand Only; Lesion 4 = Pure Agraphia on Both Sides. (After M. Rothmann, in "Handb. d. Inner. Med.," published by J. Springer, Berlin.)

Pure alexia is commonly combined with right-sided hemiopia, but right sided hemiopia does not, of itself, give rise to alexia.

In typical cases patients can write spontaneously and from dictation, especially if the writing proceed uninterruptedly. Aside from very slight word-amnesia, or paraphasia, or distortion of words on writing, at the very beginning, the other speech-functions are normal. Should these initial symptoms, however, be marked or persist, the condition is no longer pure alexia, but has to be designated "alexia, or word-blindness, with agraphia" (Déjerine), a condition that probably represents a residual stage of Wernicke's aphasia.

Pure alexia tends to persist; the outlook for recovery is very bad, though, in a few cases, improvement has been seen.

### ii. The More Complex Forms of Aphasia

Under this heading we include (1) Broca's motor aphasia, (2) Wernicke's sensory aphasia, (3) total aphasia, and (4) other complex aphasias.

#### (*1*)*Broca's Motor Aphasia* (*Cortical Motor Aphasia of Wernicke; True Cortical Motor Aphasia of Déjerine*)

In this condition, as in pure word-dumbness, there is loss of the power to speak, including all modalities of speech (spontaneous speech; power of repetition; power of reading aloud, and power of serial speech). We exclude from Broca's aphasia (1) the cases in which, from the beginning on, either the power of repetition or the power of serial speech has not been disturbed, and also (2) the cases in which either of these functions is completely restored after initial loss.

Broca's aphasia is frequently (not always) accompanied by hemiplegia, or at least by paresis of the tongue and face.

The patient is unable to indicate by pressure of the hand or by gestures the number of syllables in words (Lichtheim's test).

Whether or not the understanding of speech is at all involved in Broca's aphasia has been much disputed. As a rule, the understanding of single words is not disturbed, but there may be some impairment of understanding of the meaning of sentences (Déjerine). In testing for such impairment, for instance by asking the patient to point to parts of his own body named, we must take care not to confuse coëxisting apraxic disturbances with faulty understanding of speech (Heilbronner). In most cases of Broca's aphasia, impairment of the understanding of speech is so slight that it cannot be detected except by delicate tests. Broca's aphasia is easily separated from pure word-dumbness by the fact that, in the former, both reading and writing are disturbed, writing usually more than reading. Here, again, we must make sure that the agraphia is due neither to paralysis of the right hand nor to apraxia.

Broca's aphasia tends to persist. Through reëducation, however, motor aphasics may slowly, and laboriously sometimes, acquire a small

vocabulary; in a few cases the power of speech may be regained, even years after the insult. Sometimes the power of repetition is regained more quickly than that of spontaneous speech. In spontaneous speech, the power to name objects recovers more quickly than other powers, a fact that makes it probable that word amnesia plays no rôle in Broca's aphasia; this view is further supported by the observation that, in cases that show marked recovery, proper names are most easily pronounced; that is, words that in amnestic aphasia involve the greatest difficulty.

In the residual stage of Broca's aphasia, agrammatismus (*q. v.*) is a prominent feature. These patients speak but little, avoiding speech as much as possible, and, of this, the agrammatismus may be a sign.

### (*2*) *Wernicke's Sensory Aphasia* (*Cortical Sensory Aphasia of Wernicke; Sensory Aphasia of Déjerine*)

In this condition it is the understanding of speech that is chiefly disturbed. At first the disturbance may be as great as in cases of pure speech-deafness, but in some cases at the beginning, and in all a little later, there is evidence of some understanding of the sounds of words, and, perhaps, of the sense of words. Hemiplegia is far less common than in Broca's aphasia; but hemiopia is a frequent accompaniment, being almost always present at the beginning in cases of acute onset (Heilbronner).

Wernicke's aphasia, at its onset, is distinguishable from pure speech-deafness by the fact that there is some involvement of spontaneous speech. It can be distinguished also from convalescent cases of Broca's aphasia by the fact that, though spontaneous speech is disturbed, the patients do not avoid speech; indeed, they are often more loquacious than normal, and, once started, seem to find it hard to stop the speech-machinery. In the severe forms, there is outspoken jargon-aphasia (*q. v.*); there is an abundance of speech-impulses with a poverty-stricken vocabulary! Both distortion of words and confusion of words are common, and in these disturbances a perseveratory tendency is exhibited. In marked contrast with motor aphasia, there is, in Wernicke's aphasia, no involvement of serial speech (*q. v.*); provided, first, that the patient can be made to understand what series we wish him to repeat, and, secondly, that there be no interruption during the production of the series.

In contrast with pure speech-deafness, in which the power of repetition is lost, the sensory aphasic can repeat words, though, in doing so, there is a little verbal paraphasia and some literal paraphasia.

A remarkable feature of the sensory aphasic is his satisfaction with his speech performances. He seems not to be cognizant of the pitiable results of his efforts, and in this way is very different from the motor aphasic.

Restitution in Wernicke's aphasia occurs more often, and to a greater

extent, and, usually, more quickly, than in Broca's aphasia. There is usually marked improvement within a few weeks. The understanding of speech, the power of repetition, the power of spontaneous speech, the power of finding the words desired for use, all improve and often co-temporaneously. Though recovery may extend far, there is, in most cases at least, some residual disturbance. Sometimes word-amnesia, sometimes mild paraphasia, remains, and the patients have difficulty in understanding longer sentences and conversations in which a number of people participate. Some disturbances of reading and writing also persist.

The disturbance of spontaneous writing in Wernicke's aphasia runs more or less parallel to that of spontaneous speech. Writing to dictation is disturbed as long as understanding of word-sounds is interfered with.

The disturbances of reading in Wernicke's aphasia vary in degree. It is not common to find such great disturbance as in pure alexia. It is hard to test the elementary disturbances in alexia, owing to the lack of speech-understanding of the patients. This much can be said: in the majority of cases the understanding of what is read is more involved than the understanding of what is spoken, and the power to read aloud is more involved than the power of repetition.

### (3) *Total Aphasia*

When we have the symptoms of Wernicke's aphasia added to those of Broca's aphasia, the condition is known as total aphasia. Both the power of speaking and the power to understand speech are abolished; reading and writing are either impossible or are markedly disturbed. Sometimes the patient is capable of slavish copying; in rare cases, he may understand what he reads. In nearly every case, either hemiplegia or hemiopia is concomitant.

After a cerebral insult, total aphasia is not uncommon at the beginning, when, a little later on, the clinical findings indicate rather a Broca's aphasia or a Wernicke's aphasia; in such cases, some power of speech or some understanding of speech is usually present at the beginning, giving us a clue as to the probable further development of the case. Even in the cases in which total aphasia tends to persist, there is usually some recovery, either on the expressive or on the receptive side, most frequently the latter. As partial restitution gradually sets in, very bizarre aphasic disturbances may be met with, difficult to classify.

### (4) *Other Complex Forms of Aphasia*

Now and then one meets a patient presenting an aphasic syndrome, so different from any of the preceding simple and complex forms as to make it necessary to place it in a separate group. Of the complex forms that

from the beginning on, have lacked one or more of the essential characteristics of either Broca's or Wernicke's aphasia, at least three groups are recognizable, according as the disturbances are manifested predominantly (1) on the expressive side, (2) on the receptive side, or (3) evenly on both sides. It is interesting that these three forms correspond essentially to three varieties set up on theoretical grounds in the Lichtheim-Wernicke scheme; namely, (1) transcortical motor aphasia, (2) transcortical sensory aphasia, and (3) conduction aphasia, except that, as Heilbronner points out, the schematically deduced relations between the disturbances of reading and writing on the one hand, and the other symptoms on the other, are but little supported by clinical experience.

1. **So-called Transcortical Motor Aphasia.**—Here the disturbance is predominantly on the expressive side, and affects only spontaneous speech. The power of repetition and of serial speech is retained, or only slightly involved. Spontaneous speech may not be completely abolished, but the patients speak very little and avoid speech as much as possible, the behavior resembling that in Broca's aphasia. The condition differs from Broca's aphasia, however, in the kind of spontaneous speech possible. The patients are able to produce only small current phrases, connective words, and the like; words rich in meaning are unpronounceable. Even later on, when there has been some recovery, there is marked word-amnesia. During the stage of restitution, the speech resembles more that of a partially cured Wernicke's aphasia than that of a Broca's aphasia, but differs from that of Wernicke's aphasia in that, from the beginning on, there has been very little, if any, disturbance of the understanding of speech. The resemblance to the so-called amnestic aphasia is obvious, but in most of the cases of amnestic aphasia there has been no initial loss of spontaneous speech, so characteristic of transcortical motor aphasia. The cases are rare.

2. **So-called Transcortical Sensory Aphasia.**—This differs from Wernicke's sensory aphasia (though, otherwise, it resembles it closely) in that the power of repetition is fairly well preserved. Some would regard it as a residual stage of Wernicke's aphasia; this may be a correct view, but, if so, it is only one of the ways in which a Wernicke's aphasia may retrogress.

3. **So-called Conduction Aphasia.**—Many have doubted the justifiability of retaining this category; still, occasionally, a patient is met with in whom there is very slight, if any, disturbance of the understanding of speech, and no disturbance of the power to produce speech, as is shown by the capacity for reproducing series; the patient is fairly ready with speech, but shows a severe disturbance of spontaneous speech, with marked distortion of words (literal paraphasia) and often pronounced word-amnesia on naming objects. The symptoms vary in intensity, the whole state sometimes resembling transcortical motor, sometimes transcortical

## (e) *Table of Symptoms in the Different Forms of Aphasia*

| | Spontaneous Speech | Serial Speech | Repetition | Reading Aloud | Spontaneous Writing | Copying | Writing to Dictation | Understanding of Speech | Reading |
|---|---|---|---|---|---|---|---|---|---|
| A. *Simpler Forms* | | | | | | | | | |
| 1. Pure speech dumbness | o | o | o | o | + | + | + | + | + |
| 2. Pure speech deafness | + | + | o | + | + | + | o | + | + |
| 3. Pure agraphia | + | + | + | + | o | + | o | + | + |
| 4. Pure alexia | + | + | + | o | + | + | o | + | o |
| B. *Complex Forms* | | | | | | | | | |
| 1. Broca's motor aphasia | o | o | o | o | o | + | o | + | x |
| 2. Wernicke's sensory aphasia | x | + | o | o | x | + | o | + | o |
| 3. Total aphasia | o | o | o | o | o | + | o | + | o |
| 4. Other complex aphasias: | | | | | | | | | |
| (*a*) Transcortical motor aphasia | o | + | + | + | x | + | + | + | + |
| (*b*) Transcortical sensory aphasia | +x | + | + | + | +⁂ | + | + | + | o |
| (*c*) Conduction aphasia | +* | + | +* | +* | +⁂ | + | + | + | + |
| (*d*) Amnestic aphasia | x | + | + | + | x | + | + | + | + |

o Indicates abolished function.
+ Indicates retained function.
x Marked disturbance.
* Some paraphasia.
⁂ With paragraphia.

sensory, aphasia; so much so that the cases are often grouped with these or regarded as a combination of the two. But one symptom, particularly, differentiates them from either; namely, a marked disturbance of the power of repetition, precisely the function the integrity of which is characteristic of the transcortical forms (see cases reported by Kleist and by Heilbronner). The symptoms described by Pitres as *paraphasies* belong here. The grimacing shown by the patients on attempts at pronunciation, or at repetition, resembles that seen in Broca's aphasia, so that some cases in the literature have been wrongly classified; but the ease with which series can be reproduced excludes Broca's motor aphasia, even in its residual stage. Occasionally, the power to read aloud helps to differentiate.

4. **Amnestic Aphasia.**—This is characterized exclusively by the symptom of word-amnesia (*q. v.*). Now word-amnesia is often seen as a residue of aphasic disturbances of various sorts. The term amnestic aphasia, however, is reserved for the cases in which this symptom appears soon after the insult (without other symptoms), is very marked, and remains unchanged for some time.

### (*f*) *Lesions Causing Aphasic Disturbances*

#### i. The Motor-Speech-Center (Broca's Area)

Broca (1861), in a case of motor aphasia, found a lesion in the posterior third of the inferior frontal gyrus on the left side. This area has for decades been regarded as the motor-speech-center, and is known as "Broca's area." In 1906 P. Marie questioned the validity of this view. In his opinion, Broca's area is unimportant, motor aphasia depending rather upon lesions in the neighborhood of the nucleus lentiformis, and being in reality a Wernicke's sensory aphasia plus anarthria. This startling criticism of a generally accepted doctrine was immensely helpful, in that it led to an active re-study of the subject (v. Monakow, Déjerine, Liepmann). The tendency at present seems to be to reëstablish Broca's area as the motor-speech-center.

Modern studies have, however, shown that the area as defined by Broca is certainly too circumscribed. It is probable that the extent of the area varies in different persons, but it seems true that, in many instances, it is not limited to the gyrus frontalis inferior, but includes adjacent brain territory.

The attempts to separate a cortical from a subcortical motor aphasia clinically have not been wholly satisfactory; the findings of pathological anatomy have been conflicting. In many of the cases exhibiting clinically symptoms of the theoretical subcortical motor aphasia, the cortex has been found involved, even in cases in which the "subcortical type" appeared immediately or within a few days after the onset of the aphasia (Banti, v. Monakow and Ladame). The same criticism must be made of the sup-

posed anatomical basis of the (theoretical) transcortical form of motor aphasia. Very few cases of this form have thus far been studied by exact methods, but in at least one case so studied no definite conclusions regarding anatomical localization could be arrived at (Rothmann).

### ii. The Area Involved in Sensory Aphasia (Wernicke's Area)

In 1874, Wernicke proved the importance of lesions of the gyrus temporalis superior on the left side in the causation of his "sensory aphasia." In later studies an attempt was made to circumscribe this area to the junction of the third and fourth fifths of the gyrus, but the most careful recent studies indicate that it is as yet premature to attempt very sharply to outline the boundaries of the area. Whereas brains were formerly studied only by rough-and-ready, macroscopic methods, an aphasic brain is nowadays much more carefully analyzed, after hardening, by means of the study of serial sections stained by Weigert's method and other methods. The importance of brain territories adjacent to Wernicke's original area—namely, the transverse temporal gyri in the fossa of Sylvius, the gyrus temporalis medius, the gyrus supramarginalis, and, in some cases, the gyrus angularis—seems to have been established (Quensel).

In the attempt to separate cortical from subcortical sensory aphasia, difficulties similar to those encountered in motor aphasia have been met with. In some cases, typical clinically of the theoretical subcortical sensory aphasia, autopsy has revealed lesions in which the cortex did not participate, but in a number of other cases, slightly atypical perhaps, an involvement of the cortex of both temporal lobes has been found; moreover, subcortical lesions in the left temporal lobe are not always followed by permanent word-deafness.

An extension of the lesion from the temporal lobe in the occipital direction is suggested in the cases of sensory aphasia accompanied by marked and persistent alexia.

Attempts to localize the cases of so-called transcortical sensory aphasia have not yet been successful; it is possible that lesions behind and below the gyrus temporalis superior may be concerned (Bonhoeffer).

### iii. Other Brain Territories Concerned in Aphasic Disturbances

We have gradually learned that the form assumed, and the course followed, by an aphasic disturbance, whether motor or sensory, varies according as the lesion is limited to the motor area in the strict sense, or the sensory area in the strict sense, above mentioned, or involves other brain territories at the same time; moreover, aphasia can occur, and persist, even when neither of these two important areas is affected. The total brain territory concerned in aphasias is quite large. We may speak of it as the *aphasic region of the brain,* even though we are as yet unable

precisely to limit its borders. Probably von Monakow is not far wrong in identifying it with the total domain vascularized by branches 1-4 of the middle cerebral artery (A. cerebri media).

Broca's area and Wernicke's area lie within this great aphasic region. Other areas of special importance in it are (1) the island of Reil, (2) the temporo-occipital area, and (3) the gyrus angularis.

### (*1*) *The Island of Reil*

The *island of Reil* has often been found involved in aphasic lesions. It was for some time supposed that it is the site of lesions causing so-called "conduction aphasia," in which the chief symptom is a disturbance of the power of repetition. Later studies have shown that the power of repetition may be retained despite extensive insular lesions. Heilbronner objects strongly to the use of the term "insular aphasia," since as yet no disturbance of definite type that will permit of localizing diagnosis can be attributed to lesions of this area. This much may, however, be said; the anterior part of the island of Reil is more often found destroyed in cases of motor aphasia, the posterior part of the island in cases of sensory aphasia, whereas in some cases of total aphasia very extensive lesions involving most of the insular region have been discovered. In every case in which insular lesions exist, careful microscopical studies should be made to determine the extent and direction of the various parts of the lesion, for sometimes a narrow extension of the lesion in a given direction may be of much greater importance in accounting for the symptoms observed during life than the gross lesions that strike the naked eye at autopsy.

### (*2*) *The Temporo-occipital Area*

The posterior, or *temporo-occipital portion,* of the aphasic region seems to be especially involved in cases in which word-amnesia has been prominent, and particularly the power for naming objects. Amnestic aphasic phenomena are, however, not uncommon during recovery from aphasia due to focal lesions in various parts of the aphasic region or to diffuse atrophic processes therein.

### (*3*) *The Gyrus angularis*

The *gyrus angularis,* or its neighborhood, has been found involved in many cases of alexia. Alexic disturbances, especially the loss of power to recognize single letters, point always to a lesion in the aphasic region somewhere behind Wernicke's area, though it is not yet certain that the lesion must involve the cortex. There is some evidence, in the cases designated as "pure subcortical alexia" in which there are no accompanying agraphic disturbances, that the lesion lies deep, whereas in the cases of alexia associated with agraphia, a more superficial lesion may be suspected.

Topical diagnosis in the region just mentioned is complicated by our clinical-pathological experience of lesions in this area; they sometimes cause word-amnesia without any, or with only slight, alexia, and sometimes alexia with only slight, or without any, word-amnesia; in still other cases alexia and word-amnesia go parallel with one another. In cases of these several types, carefully studied by Quensel, no marked difference in the localization of the lesions could be made out; in certain cases with superficial lesions of the cortex, involving the white matter only slightly, no symptoms were recognizable during life.

No circumscribed localization of lesions that cause agraphic disturbances has as yet been made out, though the supposititious "cheirokinesthetic center" of Bastian may yet find its anatomical seat; Exner believed it to lie in the posterior part of the left gyrus frontalis medius, but Heilbronner saw this area occupied by an abscess in a patient whose power of writing (left-handed) was retained.

### (*g*) *Lesions Causing Agnostic Disturbances*

Here we are even less informed than for the aphasic disturbances. The different clinical forms of agnosia have already been described.

#### i. Lesions Causing Tactile Agnosia

The freer the tactile agnosia is from accompanying analgesia, the more likely it is that the lesion will be found confined to the cortex. Wernicke believed that tactile agnosia (his *Tastlähmung*) depends on lesion of the middle third of the two central gyri, but located it more in the posterior gyrus than in the anterior. According to Bonhoeffer, disturbances of tactile identification, and of the power of localization, point to injury of the cortex in the anterior central gyrus; if the lesion go deeper and further backward, the agnosia will, he asserts, be accompanied by disturbances of deep sensation (bathyanesthesia).

#### ii. Lesions Causing Auditory Agnosia (Mind-Deafness)

Clinical-pathological experience teaches that auditory agnosia points to the temporal lobe, probably to bilateral lesion, though here, also, a possible dominance of the left hemisphere has to be considered. The cases have not always been clinically differentiated from word-deafness on the one hand, or from cortical deafness on the other.

#### iii. Lesions Causing Optic Agnosia (Mind-Blindness)

It is known that this can be caused by lesions in the lateral parts of the occipital lobes, especially those involving the white matter; it does not

follow lesions confined to the regions about the calcarine fissure; these, when bilateral, cause cortical blindness, not mind-blindness. Most of the cases of optic agnosia reported have shown bilateral lesions, but it seems certain that optic agnosia can result from a unilateral lesion on the left side.

### (4) *Lesions Causing General Agnosia*

When there is a combination of tactile, auditory and optic agnosia in the same patient, the mental state is so disturbed that a clinical analysis is difficult. The condition seems to depend upon very extensive bilateral lesions involving the temporal, parietal and occipital lobes.

## (*h*) *Lesions Causing Apraxic Disturbances*

The apraxias have been subdivided by Liepmann into. (1) cortical, (2) transcortical, and (3) ideatory forms.

In *cortical apraxia* there is a defect of the psychomotor memory-pictures, which interferes with the spontaneous movements that have to deal with complicated acts.

In *transcortical apraxia,* though the spontaneous movements themselves may be undisturbed, they are not influenced normally by sense impressions, these sense perceptions having lost their determining influence upon action.

In *ideatory apraxia* there is a loss of the consciously purposeful sequence of individual acts, though each of the latter may be properly done.

Apraxic disturbances are always due to cerebral lesions above the internal capsule, a point that is of some help in the topical diagnosis of hemiplegias, since apraxia sometimes accompanies hemiplegia.

Genuine apraxia of the contralateral hand is most often caused by lesions lying behind the central gyri (v. Monakow, Bechterew, Oppenheim, Heilbronner).

An important observation of Liepmann's has shown that apraxia of the homolateral hand can be due to a supracapsular lesion in the left cerebrum, and does not necessarily point to a lesion of the right side also. Such a lesion in the left hemisphere must be such as to lead to a cutting off of the impulses that arise in the left cortex and pass through the corpus callosum to the right cortex; it may be situated either in the left hemisphere or in the corpus callosum itself. The occurrence of apraxia, or of dyspraxia, of the left hand is, therefore, sometimes of help in the diagnosis of disease of the corpus callosum.

But apraxia of the left hand may also be due to a lesion in the (contralateral) right hemisphere. It has followed, for example, a tumor in the right parieto-occipital region. Whether this injured a "praxic center" of the right hemisphere, or, instead, cut off from the latter the

fibers coming through the corpus callosum from the praxic center of the left hemisphere, remains undetermined.

There is some evidence in favor of the view that a disturbance of the power of imitating left-sided passive movements by the right hand in left-sided apraxics points to an interhemispheral lesion (corpus callosum).

In some cases a combination of agnosia and apraxia has been observed. When autopsies have been made in these cases, lesions, usually bilateral,

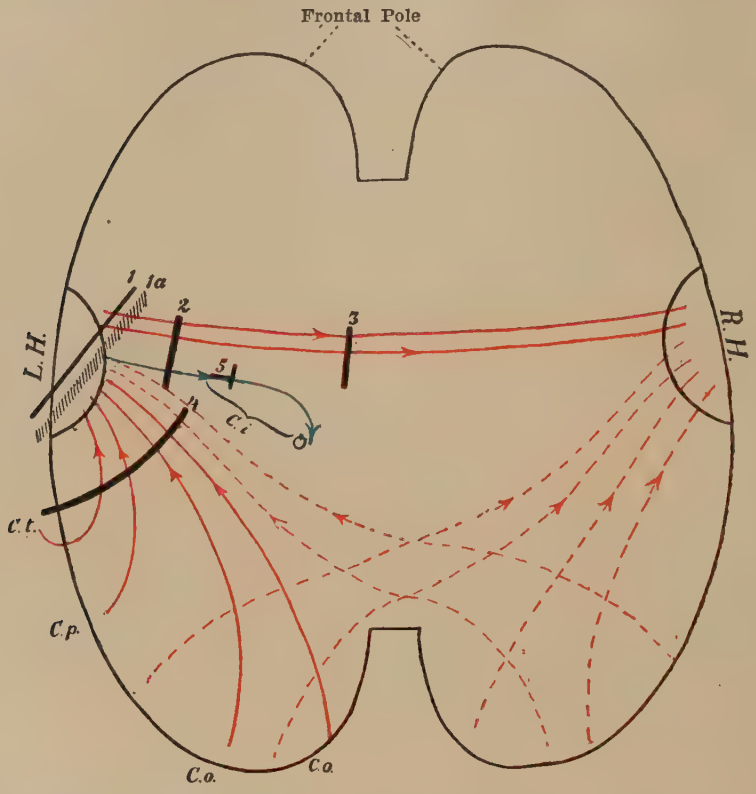


Fig. 596.—Horizontal Diagram of Apraxic Disturbances. L.H. = Center for Right Hand in Left Hemisphere; R.H. = Center for Left Hand; C.o., C.p., C.t. = Occipital, Parietal and Temporal Association Fibers to the Hand Center of the Left Hemisphere; 1 = Total Destruction of L. H., Right-sided Paralysis, Dyspraxia of the Left Hand; 2 = Right-sided Paralysis, Dyspraxia of the Left Hand; 3 = Callosal Lesion, Dyspraxia of the Left Hand; 4 = Lesion Behind the Hand Center in the Parietal Lobe; Ideokinetic Apraxia of the Right Hand, Dyspraxia of the Left Hand; 5 = Capsular Lesion, Paralysis of the Right Hand Without Dyspraxia of the Left Hand. (After Liepmann in Rothmann's article in "Handb. d. inner. Med.," published by J. Springer, Berlin.)

of variable shape have been found in the temporal, parietal and occipital lobes. In a few cases, no gross lesions were discoverable, but, instead, either an extensive brain atrophy, unevenly distributed, or "lacunar conditions in the basal ganglia" (P. Marie).

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## 7. Summary of Focal Lesions of the Hemispheres of the End Brain

We are now prepared to summarize, briefly, the localization of focal lesions in the cerebral hemispheres.

**Central Gyri and Lobulus paracentralis.**—Lesions here cause either contralateral motor, or contralateral sensory, symptoms, or both, since the general motor area, and a large part of the somesthetic area, are represented here.

Contralateral monoplegias, monobathyanesthesias, and jacksonian epilepsies are especially characteristic of lesions in this zone. Contralateral tactile agnosia and apraxia occur, especially in lesions of the left hemisphere; lesions of one hemisphere (especially the left) may also cause a homolateral apraxia or dyspraxia, possibly also a homolateral tactile agnosia.

**Frontal Lobe.**—Lesions at the foot of the gyrus frontalis inferior on the left side (Broca's area) in right-handed people cause Broca's motor aphasia; a subcortical lesion here causes pure word-dumbness. Tumors

in the anterior part of the frontal lobe are sometimes accompanied by a tendency to make witticisms (*Witzelsucht*).

**Parietal Lobe.**—Lesions in the anterior part cause contralateral somesthetic disturbances, especially in the domain of deep sensibility; also tactile agnosia and apraxia.

Lesions in the gyrus angularis of the left side cause optic aphasia, or alexia; if the lesion go deep enough to injure the occipitothalamic radiation it causes hemi-anopsia. Lesions here also interfere with voluntary associated movements of the eyes to the side; in destructive lesions, the eyes look toward the lesion; in irritative lesions, away from it.

**Temporal Lobe.**—Lesions in the posterior half of the first temporal gyrus (Wernicke's area) cause Wernicke's sensory aphasia; a subcortical lesion may cause pure speech-deafness (word-deafness).

Bilateral destruction of the first temporal gyrus and of the transverse temporal gyri (auditory sense areas) causes cortical deafness; larger bilateral lesions situated in the lower parts of the temporal lobes cause auditory agnosia (mind-deafness).

Irritative lesions in the uncus give rise to uncinate gyrus fits (hallucinations of smell and taste, with smacking of the lips, and tongue movements).

**Island of Reil.**—Lesions here cause complex aphasias; lesions of the anterior part cause aphasias resembling Broca's motor aphasia; lesions in the posterior part cause aphasias resembling Wernicke's sensory aphasia; lesions in the island have also been held responsible for the transcortical aphasias (motor and sensory), and for the conduction aphasia of Wernicke.

**Occipital Lobes.**—Lesions of the cortex about the calcarine fissure give rise to hemi-anopsia; bilateral destruction causes cortical blindness. Lesions marginal from this in the occipital lobe, and especially bilateral lesions of the lateral surface of the lobes, cause visual agnosia (mind-blindness).

**Centrum semi-ovale.**—Lesions in the centrum semi-ovale interfere either with projection systems (motor or sensory), or with association systems, according to their size and location (monoplegias, mono-anesthesias).

**Corpus callosum.**—Lesions here give rise to apraxic disturbances (*q. v.*).

## F. Topical Diagnosis of Lesions of the Cerebellum and of its Peduncles

Lesions involving the cerebellum may cause (1) symptoms due to injury of the cerebellum itself or its peduncles, or (2) "neighborhood

symptoms," from pressure upon other parts (medulla oblongata, pons, midbrain, vena magna Galeni).

## 1. Symptoms Due to Injury of the Cerebellum Itself, or of Its Peduncles

Lesions of the worm (vermis) cause disturbances of equilibrium (cerebellar ataxia), vertigo and paroxysmal vomiting.

Lesions of one lateral lobe, say, of the right hemisphere of the cerebellum, or of the middle cerebral peduncle on the right side (brachium pontis), if irritative, will cause a rotation of the body in the direction of unscrewing an ordinary screw, the patient's head being the head of the screw; if destructive, there will be tendency to rotation in the reverse direction—namely, that of screwing in a screw—owing to tonus and hemiparesis of muscles on the right side. There may also be nystagmus, and skew-deviation, in addition to homolateral asthenia, hypotony, ataxia and adiadochokinesia. Cerebellar ataxia and cerebellar asynergy have already been fully discussed (see Disturbances of Motility).

Large lesions of the cerebellum, causing destruction of considerable portions of the organ, are sometimes observed at autopsy, when, during life, no symptoms pointing to them have been observed; this is especially true of congenital lesions, and of lesions occurring in early childhood (Spiller, Wadsworth). In my study of the brains of two brothers that had hereditary cerebellar ataxia (observed *intra vitam* by Sanger Brown) there were extensive lesions of both the spinal cord and cerebellum.

It is practically important (1) in unilateral lesions to determine (a) the side of the lesion, and (b) whether it be extracerebellar (*e. g.,* tumor of cerebellopontile angle), or intracerebellar—not always an easy matter; and (2) when the symptoms are bilateral, to decide whether (a) the vermis is affected, or (b) both lateral lobes are involved, and, in either case, whether the lesion be inside or outside the organ (meninges, fourth ventricle). In all these cases the functions of the vestibular nerves should be carefully studied by Bárány's method (See Vestibular Syndromes).

Lesions of one *inferior cerebellar peduncle* (corpus restiforme) may cause either (1) cerebellar ataxia with lateropulsion, *i. e.,* falling toward the side of the lesion (direct cerebellar tract), or (2) a homolateral movement-ataxia (fibers from posterior funiculi of the cord).

Lesions of the *middle cerebellar peduncle* (brachium pontis) may cause an ataxia due to deprivation of the cerebellar hemisphere of the cerebral impulses that come to it by way of the collaterals from the pyramidal tract to the nuclei pontis.

Lesions of one *superior cerebellar peduncle* (brachium conjunctivum) may cause unilateral chorea, and ataxia of the cerebellar type (path from cerebellum to red nucleus).

Symptoms pointing to the cerebellum may be due to meningitis serosa circumscripta of the lateral cistern (*q. v.*).

## 2. Pressure Symptoms from Cerebellar Lesions

These may be either general symptoms of increased intracranial pressure (choked disk, headache, vomiting, disturbances of consciousness, etc.); or they may be "neighborhood symptoms," due to pressure on adjacent structures. The latter include:

1. Midbrain symptoms (eye-muscle paralyses, conjugate deviation, nystagmus).

2. Pontile symptoms (paralysis of associated ocular movements; paralysis of M. rectus lateralis; alternating paralysis of N. facialis and N. abducens; involvement of N. trigeminus, N. cochleae, and N. vestibuli).

3. Symptoms referable to the medulla oblongata (N. glosso-pharyngeus, N. vagus, N. accessorius, N. hypoglossus).

It is probable that before long the results of the studies of Horsley and Clarke, with precise local electrical stimulation of the cerebellum, and the exact anatomical studies of Bolk upon the cerebellum, can be better utilized for the topical diagnosis of cerebellar diseases.

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# Part XII

SECTION III

## DIAGNOSIS OF THE NATURE OF A NERVOUS DISEASE (SPECIAL DIAGNOSIS)

Having made a systematic examination of the various nervous functions (Accumulation of Data), and having drawn what inferences are possible regarding the neuron systems involved, that is to say, regarding the site of the lesion (Topical Diagnosis), we have next to try to decide upon the nature of any nervous disease present (Special Diagnosis).

## A. Classification of the Nervous Diseases

It is customary to subdivide nervous and mental diseases into those that are functional and those that are organic, the former having no anatomical lesions demonstrable by our present methods of examination.

In both the functional and the organic disorders, our exact diagnosis as to the nature of the malady depends upon (1) studies of the cause (etiology), (2) of the mode of onset and the course of the symptoms, and (3) of accompanying phenomena in other parts of the body. Clinical observations, laboratory studies, and pathological examinations have yielded us a body of facts that permit us to draw conclusions regarding the nature of a disease process.

### 1. Organic Nervous Diseases

From pathological-anatomical studies, we may classify the organic diseases of the nervous system as follows:

(a) Disturbances of development.
(b) Disturbances of circulatory origin.
(c) Disturbances of metabolism.
(d) Inflammatory diseases.
(e) Regenerative and adaptive processes.

(f) Disturbances of lumen.
(g) Disturbances of continuity.
(h) Invasions by animal parasites.
(i) Tumors.

## 2. Functional Nervous Diseases

The so-called functional disorders include (1) the various neuroses (psychoneuroses, angioneuroses, trophoneuroses), and (2) the non-organic psychoses.

# B. Disturbances of Development of the Nervous System (Malformations)

Many of these are of interest chiefly to the obstetrician (anencephalic monsters, hemicephaly, meningocele, spina bifida, rhachischisis).

Other anomalies of development are of more interest to the neurologist and the general practitioner. Among them may be mentioned microcephaly, porencephaly and cerebral agenesia.

Fig. 597.—True Microcephaly. (After Knoblauch in R. Bing's article in "Handb. d. inner. Med.," published by J. Springer, Berlin.)

## 1. Microcephaly

In this condition, the cerebrum is abnormally small and is enclosed in a small skull. The cerebellum may be of normal size. The projection systems are less defective than the association systems.

## 2. Porencephaly

In this condition there are partial defects of the brain with loss of single parts.

There may be a primary porencephaly due to early embryonic lesion, or a secondary porencephaly (pseudoporencephaly), often due to trauma at birth, interfering with the blood supply. All cases of porencephaly —both true and false—stand in relation to the arterial supply of the cerebrum, most often to the A. cerebri media (See Cerebral Palsies of Children).

## 3. Cerebral Agenesia; Microgyria; Lobar and Tuberous Sclerosis

Many cases of idiocy and imbecility depend upon anomalies of development (agenesias, microgyria) of the cerebral cortex. Lobar sclerosis represents a gliotic shrinking and hardening of the whole of one or both hemispheres (P. Marie). Tuberous sclerosis is a gliomatosis, which may be neoplastic, though this is not certain (Vogt). Nut-sized firm masses, often quite prominent, are visible in the cortical substance, especially of the central gyri; they consist of masses of glia fibers and glia cells.

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# C. Diseases of the Nervous System of Circulatory Origin

These include anemia, hyperemia, edema, hydrops, cerebral atherosclerosis, hemorrhage, thrombosis, embolism and aneurism. We shall discuss the diagnosis of the most important conditions only.

## 1. Clinical Syndromes Due to Atherosclerosis of the Blood Vessels of the Nervous System

Atherosclerosis is a disease of advanced life, often insidious in onset, with headache, vertigo, and mental disturbances. It may lead to cerebral hemorrhage (apoplexy), or to softening (thrombosis, embolism); and it may cause sudden death, or permanent paralyses.

Atherosclerosis of cerebral and spinal blood vessels is responsible for the majority of nervous and mental diseases developing after the age of fifty years. The somatic and psychic symptoms cover the widest possible range, since lesions due to arteriosclerosis occur in all parts of the nervous system; but as these lesions are of certain general types and affect certain areas preëminently, it is possible to distinguish in the symptomatology certain clear-cut clinical syndromes.

Arteriosclerosis of the nervous system may be only a part of a general arteriosclerosis or it may occur in cases in which the radials, aorta, etc., show little, if any, sclerotic change. It may accordingly occur alike in cases with and without hypertension.

The type of atherosclerosis that affects the blood vessels of the nervous system does not differ essentially from that seen in blood vessels elsewhere. The distribution of the sclerotic process in the vessels of the brain and cord has been shown to be quite variable; the large vessels of the base of the brain or of the pons, the medulla or the spinal cord may be chiefly affected, or the smaller arteries supplying the cortex, the subcortical areas, or the basal nuclei may alone exhibit marked change. The changes in the nervous tissue secondary to arteriosclerosis consist in diffuse atrophic changes due to the interference with nutrition and of lesions of a more focal nature about the affected vessels, perivascular gliosis, macular atrophies of the cortical substance, and peri-arteriolar lacunae. Aside from these more usual effects of arteriosclerosis, two types of accidental lesions are especially apt to occur: hemorrhage into the brain-tissue as a result of rupture of an artery or of a miliary aneurism, and areas of ischemia of brain tissue with softening, due to arterial thrombosis. The extent of the hemorrhage, or the situation of the thrombus, determines the extent of the focal lesion of nervous tissue.

### (*a*) *Pseudobulbar Paralysis*

Cerebral atherosclerosis is the usual primary cause of *pseudobulbar paralysis* in adults. This symptom-complex results from *injury to the*

*supranuclear paths* going to the motor nuclei of the cerebral nerves. Multiple, bilateral foci are necessary for its production. The focal lesions may be areas of softening, scleroses, hemorrhages, cysts, etc. The patients suffer from several cerebral insults. The usual history is of a hemiparesis (right or left), involving the face and tongue, being followed by a second ictus with development of hemiparesis on the opposite side. Coincidentally with these events, paralysis, or paresis, of all voluntary movements of the lips, tongue, jaws and pharnyx occurs. Saliva drools from the mouth. There is dysarthria (monotonous, nasal speech) dysmasesia and dysphagia (difficulty in mastication and in deglutition, regurgitation of fluids through the nose). Spasmodic, involuntary laughing and crying are characteristic symptoms, and in the performance of these reflex acts no paralysis of the facial muscles is evident. There is neither atrophy, nor DeR in the muscles affected. The masseter reflex is increased; rarely true persistent trismus occurs.

The usual initial bilateral hemiplegia may partially or wholly clear up in the extremities. Commonly, however, there remains a spastic paraparesis of the lower extremities (*vide infra*). The psychic condition depends upon the degree of cortical involvement. In some cases the intelligence is very little affected. Usually, there is gradually developing apathy, confusion and dementia. Aphasia is common.

The history of onset with ictus, the evidences of arteriosclerosis and the symptoms referable to the upper neurones rather than the lower, easily distinguish the affection from true bulbar paralysis.

The effects on the functions of the nervous system of these varied diffuse and focal lesions may be apparent in both the psychic and somatic processes of the patient. In the psychic sphere, characteristic changes in mentality accompany the lesions of the cortical tissue. They vary from the milder cases that present a picture simulating neurasthenia to those cases that, as a result of repeated destruction of small areas of nervous tissue, show the most profound dementia. Deficiency-phenomena form the basis of the mental changes in these cases. The somatic manifestations on the sensory and motor sides are infinitely varied according to the sites of the focal lesions. The motor symptoms are usually more pronounced than the sensory. Hemiplegia, paraplegia, pseudobulbar palsy, athetosis, and jacksonian epilepsy are among the more common results.

Certain of these multitudinous psychic and somatic symptoms occur in association with sufficient regularity to merit description as distinct clinical syndromes, but it should be remembered that the disease process is essentially the same in all and hence marked overlapping is to be expected and to be looked for. Of these syndromes, pseudobulbar paralysis, senile spastic paraparesis, cerebral hemorrhage, and cerebral thrombosis are all well-characterized. The occurrence of an initial ictus of greater or lesser severity lends a certain unity to the history of these clinical types.

Among the cases in which the symptoms are more exclusively mental, a milder form in which no evidence of ictus is apparent is to be distinguished from the more severe progressive form with the history of repeated slight ictus, and from dementia following a single large apoplexy.

**Senile Spastic Paraparesis.**—The tendon reflexes are commonly exaggerated in cases of cerebrospinal arteriosclerosis. In certain cases there is a gradual development of a true spastic paraparesis of the lower extremities (increased muscle-tonus, patellar and ankle-clonus, Babinski's sign). The sphincter reflexes may, or may not, be affected. The condition may be due to bilateral hemiplegia or hemiparesis, or to periarterial lacunae or other focal lesions involving the pyramidal tracts in the spinal or intracranial portions of their course.

The patient complains of weakness in the lower extremities and uses a cane to support himself. The steps are short and the feet are scarcely lifted from the ground (*démarche à petit pas* of Charcot). Frequently there is a degree of uncertainty in the movements, which becomes especially apparent if the patient be commanded to turn quickly. Romberg's sign, however, is not present. Sensory changes are absent or slight. Evidences of cerebral arteriosclerosis are usually present (mental deterioration, pseudobulbar palsy, aphasia, etc.)

The *differential diagnosis* must be carefully made from paraplegia due to pressure (cord tumor, Pott's disease, bone-metastases of carcinoma) or as a part of an amyotrophic lateral sclerosis. Hysterical basophobia is not uncommon in the aged, but does not present the signs of an organic paraplegia. The two conditions may, however, occur in association.

### (*b*) *Cerebral Hemorrhage*

(*Apoplexy*)

This is usually due to atherosclerosis, in persons aged fifty or more. The onset is usually sudden, the patient falling unconscious (apoplectic insult); or there may be only a brief vertigo at the time of the hemorrhage. The size and the position of the hemorrhage determine the symptoms. Hemorrhages occur most frequently in the region of the central ganglia and of the internal capsule, but hemorrhages in the centrum semi-ovale, in the cortex and in the pons are not uncommon. Large hemorrhages may break into a ventricle.

The most common after-effect of apoplexy is contralateral hemiplegia with loss of the cremaster and the abdominal reflex, and with positive Babinski- and Oppenheim-signs on the paralyzed side. Sometimes there is conjugate deviation of the eyes, the head and eyes being turned toward the lesion. Later on, there may be partial recovery from the hemiplegia; often contractures develop. For the focal symptoms due to hemorrhage in different parts of the brain, see Topical Diagnosis.

Cerebral hemorrhage is to be looked upon as an accident due to the existence of an underlying cause, which, in older people, is usually cerebral atherosclerosis. Apoplexy is simply the major form of the cerebral insults that are characteristic of this condition. All cerebral arteriosclerotics are prone to suffer from repeated slight ictus, the symptoms

of which are most various. A sudden attack of vertigo, a transient aphasia, an amnesia, a hemiparesthesia or a hemiparesis clearing up in a few hours or days, may occur as an incident in the history of such cases. The pathological basis of such phenomena is not well established. By some it is held to consist of spasm of the diseased vessels, by others capillary hemorrhages, or small thromboses are held responsible. The popular term "warnings," applied to such symptoms, is justified by the clinical observation that such cases are especially prone to suffer with "apoplexy" later, due to severe cerebral hemorrhage.

The ictus due to cerebral hemorrhage, and the paralytic sequelae of the destruction of nervous tissue form, together, a characteristic clinical picture.

The shock of the onset of the hemorrhage usually leads to rapid loss of consciousness. The patient lies in deep coma for from a few hours up to several days or even weeks if death does not occur. If the hemorrhage be of considerable extent, and especially if there is bleeding into the ventricles, signs of increased intracranial pressure soon appear (disturbances in respiration, especially Cheyne-Stokes breathing, rapid increase in the blood pressure, if this was not previously elevated, and, in some instances, bradycardia). Where these symptoms come on quickly and are marked, death is the usual result. Hyperpyrexia may also occur as a result of disturbance of the thermal regulating center. A mild grade of choked disk may be secondary to pressure due to hemorrhage. In most cases recovery of consciousness occurs gradually, the patient passing through a confused state in which he is often very restless and antagonistic.

Hemorrhages may occur in any region of the brain, and focal symptoms of the most varied nature may result. In by far the greater number of cases, however, the pyramidal tracts are involved, causing a development of a contralateral hemiplegia.

The hemiplegia due to cerebral hemorrhage usually appears at the time of, or shortly after, the initial ictus. Rarely, it develops slowly in the course of a number of hours. The paralysis is usually flaccid at first, the affected cheek puffs out with each breath, the lifted limb drops quite limp. Spasticity appears at the end of a variable number of days and either remains permanently, or is gradually lost with the return to a normal condition. In some cases, however, an early rigidity is observed in the first day, which may, later, change to a flaccid and, still later, to a spastic condition. Clonic twitching movements in the paralyzed side are occasionally seen at the onset, or later a hemichorea may be observed. But such signs of an irritative lesion are more common in thrombosis.

The tendon reflexes are often all absent during the depth of the comatose stage and, in almost all cases, are diminished on the paralyzed side during the early days. Later, when spasticity is present, they are of course increased and patellar and ankle-clonus can usually be obtained. Babin-

ski's sign on the paralyzed side is present throughout, except while the coma is profound. The superficial abdominal and cremasteric reflexes are abolished. There may be retention of urine at first, necessitating catheterization, but usually reflex emptying of the bladder occurs during the comatose state, and, later, there is recovery of voluntary control. The pupils during deep coma do not respond to light; later, the pupillary reflexes are normal.

The distribution of the paralysis in hemiplegia has been carefully studied by Beevor. Its extent depends upon the area involved by the cerebral lesion, but certain movements on the paralyzed side show a strong tendency to be partially or wholly retained. The muscles concerned with these movements are perhaps bilaterally innervated. Such muscles are the eye-muscles, laryngeal muscles, the muscles of the back, neck and chest, and, to a lesser extent, the upper facial muscles and the muscles of mastication.

Recovery from hemiplegia, when it occurs, always begins within the first month, though it may continue gradually over a long period of time. Recovery in the leg is usually more complete than in the arm. In well-developed cases of hemiplegia, complete recovery is rare. The occurrence of *contractures* tends to limit the regaining of complete function. It is these contractures that give to the old hemiplegic his characteristic appearance. Contracture of the lower facial muscles draws the corner of the mouth to the paralyzed side. The arm is flexed at the elbow and held stiffly adducted against the chest wall, the forearm is half-way between pronation and supination and the fingers are flexed. The leg is extended and rotated medialward. The gait is characteristic; the paralyzed leg is stiffly swung forward, the toes and outer margin of the foot scraping the ground.

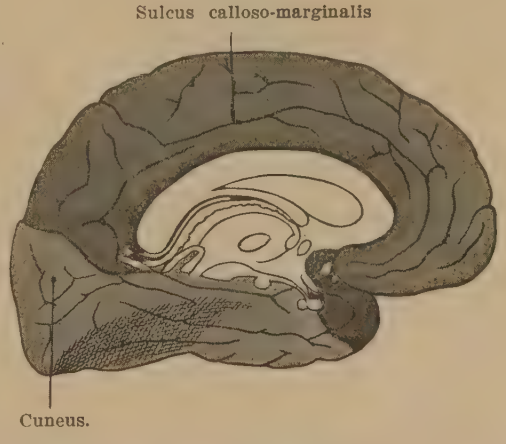


Fig. 598.—The Superficial Distribution of the Larger Cerebral Arteries. Light Black: Anterior Cerebral Artery; Dark Black: Middle Cerebral Artery; Gray: Posterior Cerebral Artery. (After Poirier from Corning in O. Veraguth's "Die klin. Untersuch. Nervenkr.," published by J. F. Bergmann, Wiesbaden.)

Sensory and trophic symptoms on the paralyzed side are of less importance, though a partial anesthesia will almost always be found on careful examination during the earlier stages. Sensation is usually rapidly recovered. Edema of the paralyzed extremities is common.

Mention should be made of *aphasia,* which is commonly associated with right-sided hemiplegia. It is discussed elsewhere. Postapoplectic dementia of various grades of severity is also a frequent residuum after cerebral hemorrhage.

**Differential Diagnosis.**—We must exclude (1) simple *syncope* (temporary cardiac disturbance); (2) *epilepsy* (convulsion preceding coma, biting of tongue, absence of hemiplegia, age of patient); (3) a paralytic attack in the course of a *dementia paralytica* (anamnesis, course, Argyll-Robertson pupils, cerebrospinal fluid, Wassermann); (4) *hysterical states* (normal reflexes, facial expression, psychogenic influences); (5) *uremic coma* (previous history, edema, albuminuric retinitis, slow onset, often with vomiting and convulsions); (6) *cerebral softening* due to embolism or thrombosis (often difficult to differentiate; patient usually younger with vomiting and convulsions); (6) *cerebral softening* due to embolism (arterial hypotension favors thrombosis; monoplegias and aphasias are more common than hemiplegia).

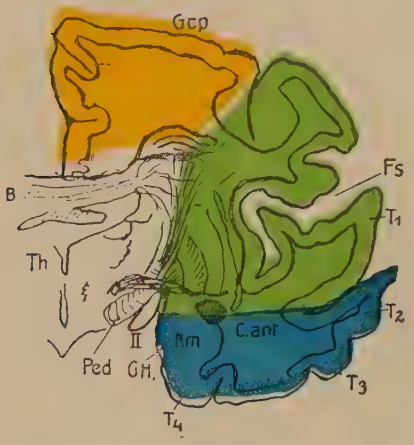


Fig. 599.—The Blood Supply of the Deeper Portions of the Brain on Frontal Section. Yellow: Ant. Cerebral Art.; Green: Mid. Cerebral Art.; Blue; Post. Cerebral Art. The Choroid Artery (Not Shown) Also Helps to Supply the Posterior Part of the Midbrain. Gcp = Gyr. centr. post.; Fs = Fissura Sylvii; $T_{1, 2, 3, 4}$ = 1-4 Temporal gyri; C. ant. = Ant. horn; Am = Nucleus amygdaloid; GH = Gyr. Hippocampi; Ped = Peduncle; Th = Thalamus; B = Corpus callosum. (After v. Monakow in O. Veraguth, "Die klin. Untersuch. Nervenkr.," published by J. F. Bergmann, Wiesbaden.)

### (c) *Cerebral Softening*

*(Cerebral Embolism, Cerebral Thrombosis, Encephalomalacia)*

Softening may be due either to thrombosis, or to embolism, of a cerebral artery. Emboli most often lodge in the left middle cerebral artery, or one of its branches. Thrombi form most often in the large arteries at the base (middle cerebral, internal carotid, etc.) or in one of their branches.

**Symptoms.**—If a large vessel be occluded, the symptoms may resemble those of an apoplectic insult, but the coma may be absent or it is less deep, and briefer. In embolism, the onset is extremely sudden (often in the early morning); in thrombosis, the onset is gradual, sometimes extending over days, or weeks. Hemiplegia, monoplegia, aphasia, hemianopsia, hemi-anesthesia, etc., appear depending upon the brain territory that becomes necrotic owing to cutting off of the blood supply of the artery occluded.

**Differential Diagnosis.**—(1) From *cerebral hemorrhage* (*q. v.*); (2)

from tumor cerebri (in the latter, signs of increased intracranial pressure, such as choked disk, slow pulse or vomiting); (3) from *abscess* (*q. v.*); (4) from *neurosis.*

### (*d*) *Aneurisms of the Intracranial Arteries*

These are rare. They occur most often at the base (A. cerebri media; A. basilaris). They may be due either to lues (luetic arteritis) or to atherosclerosis.

**Symptoms.**—These consist largely of the signs of increased intracranial pressure (headache sometimes pulsating, vertigo, vomiting, dulling of consciousness, but rarely choked disk). On auscultation, a loud murmur may be audible over the whole skull, or in a localized area. Local compression, especially at the base of brain, may cause lesions of the cerebral nerves, or of long tracts in the medulla and pons.

### (*e*) *Mental Disturbances Due to Arteriosclerosis*

Two main forms of arteriosclerotic change in the brain are now distinguished by the pathological anatomists; namely, (1) changes in the vessels of the brain stem, and (2) changes in the vessels of the cerebral cortex and centrum semiovale.

The coarser forms of arteriosclerosis of the cerebral vessels tend to involve especially those at the base of the brain and give rise to gross neurological lesions rather than to mental changes. If mental changes are present, they are usually due to complication of the process in the basal vessels by changes in the vessels of the cortex (Campbell; Jacobsohn).

The mental changes due to arteriosclerosis of the cortical vessels have been studied especially by Klippel (1895) in France, and by Binswanger and Alzheimer (1894-1909) in Germany.

Through these studies, the mental disturbances due to arteriosclerosis have been sharply separated from those somewhat similar disturbances met with in some forms of dementia paralytica and in senile dementia. As a rule the diagnosis can be made with certainty during life.

The sclerotic change may affect predominantly the short arteries of the cortex or the longer vessels of the white matter; in the latter instance, the condition has been described as *encephalitis subcorticalis chronica.* When the cortical vessels are chiefly involved, there may be (1) slight diffuse changes in the cortical tissue, (2) a perivascular gliosis, or (3) macular atrophies of the cortical substance (senile cortical atrophy of Alzheimer).

The initial symptoms of cerebral arteriosclerosis correspond to the *nervous form of arteriosclerosis of Windscheid,* of which the three cardinal symptoms are headache, vertigo, and enfeeblement of memory. The patients tire easily, especially when trying to do mental work. The condition is most often mistaken for (1) simple neurasthenia, or (2) the early stage of dementia paralytica.

In the *severer progressive forms of cerebral atherosclerosis,* the above mentioned initial symptoms may gradually go over into severer symptoms, or the disease may begin with an apoplectic attack, followed by severe mental symptoms. As the disease progresses, the patients suffer attack after attack in which mental and neurological symptoms become more pronounced; indeed, emphasis is to be laid upon the fact that these patients seem to suffer from "brain-disease" rather than

from "mental disease." An arteriosclerotic dementia gradually develops. The psychic fatigability becomes associated with difficulty of comprehenson and of attention, with slowing of associations and tendency to mental perseveration. The recording faculty is early involved. A characteristic feature is the maintenance of good judgment regarding many things, with loss of judgment in certain definite directions (*démence lacunaire*). The patients are usually depressed, lose emotional control easily, even weeping without provocation. At times the patients are irritable or even violent. Sometimes they are anxious and show suicidal tendencies, though this is not common. Often there is painful insight into the deterioration. Despite these symptoms, the patients are often excessively dull and indifferent regarding other matters that normally would cause emotional reactions. This apathy is frequently accompanied by an emptiness of countenance. Sometimes the disease sets in with a melancholic state that may be mistaken for a manic-depressive psychosis until the later dementing process makes the etiology clear. The signs of arterial hypertension and the atherosclerotic changes in the heart and kidneys are often helpful in diagnosis, though it must be remembered that cerebral atherosclerosis may run its course without arterial hypertension.

A considerable proportion of the cases of epilepsy beginning in later life (*epilepsia tarda*) are due to atherosclerosis of the vessels, or its accompanying perivascular gliosis. Patients are met with in whom *petit mal* attacks, quite like those of idiopathic epilepsy, may occur for months or years before their atherosclerotic origin is definitely recognizable. These minor attacks may consist of temporary vertigo, of *petite absence,* or of localized twitchings. Such symptoms are especially prone to occur in atherosclerosis accompanied by alcoholism (Redlich; Kraepelin). Alzheimer has described a cardiovascular epilepsy, which he assumes to depend upon circulatory changes in the brain secondary to atherosclerotic changes in the heart.

In the *encephalitis subcorticalis of Binswanger,* partial defects of intelligence occur early (cortical blindness, cortical deafness, asymbolia, sensory aphasia, motor aphasia, amnestic aphasia), associated with monoplegia or hemiplegia, imperative laughing and crying, hemi-anopsia, etc.

### (*f*) *Senile Dementia*

Normally, in old age, the circle of ideas becomes circumscribed; there is loss of mental elasticity, and impoverishment of interests, a dulling of the affective life, an impairment of the recording faculty, and the appearance of unpleasant ethical peculiarities, with exaggeration of the ego. The patients become hypochondriacal, suspicious and stubborn.

But a group of cases has been recognized in which these changes occur much earlier in life than on the average, and they are described in the literature as *senile dementia.* In the brains of such persons *post mortem* there is a quantitative increase of those changes in the cortex that are met with in physiological senility. These changes include fatty degeneration of the nerve cells, lipoid accumulations in the glia cells, increase in the glia fibers on the surface of the cortex, regressive changes in the walls of the blood vessels, and increase in the number of the Redlich-Fischer plaques. Alzheimer has also described a peculiar change in the neurofibrils.

Among the earliest symptoms manifested by these patients are certain ethical and esthetic defects. There is a pathological increase in the mental peculiarities that characterize the physiological senium. Indifference to surroundings, lack of consideration for others, limitation of interests to gross bodily needs, disregard for neatness, cleanliness and orderliness, growth of stubbornness, inaccessibility to

persuasion, tendency to pedanticism and peevishness, and hypochondriacal complainings, are characteristic. Sometimes there is a tendency to silliness, erotism, foolish love-making, unwise marriage, or to sexual misdemeanors (Spielmeyer). Mental enfeeblement and defective judgment gradually increase. The impairment of the recording faculty becomes ever more noticeable and the interest of the patient ever more limited to events in earlier life. Restlessness at night is a common symptom, the patients wandering about the house and busying themselves with occupations that properly belong to the day-time.

Though this peculiar mental enfeeblement, characterized by impairment of the recording faculty and of the memory and by increasing difficulty and slowness in grasping new impressions from the outside is especially characteristic of senile dementia as a whole (Kraepelin), a number of subforms have been described, including:

(1) Wernicke's *presbyophrenia* (marked disturbances of the recording faculty with retention, for a long time, of orderly thought and judgment; tendency to temporal disorientation and to confabulation).

(2) Binswanger's *dementia praesenilis* (dementia beginning between 40 and 50; development of apathy, loss of memory, disturbances of speech and gait, egocentricity, conflicts with surroundings; distinguishable from ordinary senile dementia by congenital mental inferiority and by the early development of outspoken dementia; distinguished from dementia paralytica by negative Wassermann reaction, negative somatic signs, and by the long duration).

(3) Certain *atypical forms of senile dementia,* including (a) the *circumscribed senile brain atrophy* of Pick, in which a senile dementia is accompanied by a left-temporal-lobe syndrome causing aphasia, agraphia or alexia, and (b) *Alzheimer's disease* (Kraepelin), in which there is a slow development of severe dementia along with fading phenomena of organic disease of the brain. The dementia reaches a high grade and associated with it are focal phenomena causing asymbolic, aphasic and apraxic disturbances (Spielmeyer). The condition is distinguishable from cerebral atherosclerosis by the fact that apoplectiform attacks do not contribute to the occurrence of the high grade of dementia and the focal symptoms; alterations in the mental state develop gradually and not paroxysmally; moreover, the signs of atherosclerosis elsewhere in the body are usually absent. Dementia paralytica can be ruled out by a study of the blood and of the cerebrospinal fluid.

## 2. Sinus Thrombosis

This may be marantic in origin (cardiac weakness, cachexia, chlorosis), or be due to inflammation (most often, by extension from a mastoiditis).

**Symptoms.**—There is stasis in the veins of the skull and of the face, depending on the sinus affected; (1) in thrombosis of the sinus cavernosus, the stasis affects the frontal veins and the orbital veins, causing exophthalmos; (2) in thrombosis of the sinus transversus, there is edematous swelling of the soft parts behind the mastoid and dilatation of the veins of the skin; there may be an extension of the thrombus to the jugular vein (palpation).

## 3. Gas Embolism of the Cerebral Arteries

*(Caisson Disease, Diver's Disease)*

Divers, or workers in caissons, under pressure of three to four atmospheres, if they return too suddenly to normal atmospheric pressure, suffer from cardiac and respiratory disturbances, and from gas embolism, with ischemic softening of the brain or cord (cerebral paralyses, transverse lesions with paraplegia). (See Part IV.)

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## D. Diseases of the Nervous System Due to Disturbances of Its Metabolism

*(Atrophies and Degenerations)*

**Neuronal Degenerations.**—If the axon of a neuron be interrupted, the distal portion, with its myelin sheath, undergoes complete degeneration

(wallerian secondary degeneration or cellulifugal degeneration). If the terminals of an axon be destroyed, there also occurs, proximal to the lesion, a slow, retrograde, indirect or cellulipetal degeneration (Gudden's atrophy). Both forms of degeneration are met with in diseases of the spinal cord and brain, injuries to the motor or centrifugal paths causing *descending secondary degenerations,* injuries to the sensory or centripetal paths causing *ascending secondary degenerations.* In the peripheral nerves, after trauma or necrosis, secondary degeneration also occurs.

In certain diseases, toxins are produced that have an elective affinity for certain neuron systems. Injuring these, they give rise to specific degenerations (so-called *system diseases*). Such system diseases may effect the motor neurons, the sensory neurons, or the sensory and motor neurons simultaneously.

## 1. Degenerations of the Motor Neuron Systems or of the Muscles They Innervate

If we think of the motor conduction path as the corticomuscular path from the motor area of the cerebral cortex to the voluntary muscles, we may classify the diseases directly affecting this system into (1) primary diseases of the muscles themselves (dystrophies, or primary myopathies); (2) degenerations of the lower motor neurons (neurotic muscular atrophy, progressive muscular atrophy, and bulbar paralysis); (3) degenerations affecting lower motor neurons and upper motor neurons simultaneously (progressive central muscular atrophy, and amyotrophic lateral sclerosis); (4) degenerations affecting upper motor neurons (or pyramidal tracts) alone (primary lateral sclerosis).

### (*a*) *The Primary Myopathies*

(*Dystrophia musculorum progressiva; Progressive Atrophic Myopathy; Protopathic Muscular Atrophy*)

In reality, these are diseases of the muscles, rather than of the peripheral nerves or nerve centers, but their diagnosis may be most conveniently considered here, in connection with the other forms of muscular atrophy. The disease begins in childhood, or in youth; it occurs in families; it involves first the muscles of the pelvic girdle and of the lumbar region, then those of the shoulder girdle, and it affects the muscles of the upper arm and of the thighs (proximal portions of extremities) before the more distal muscles become involved. The atrophy may be combined with true hypertrophy of some parts, more often with pseudohypertrophy (fat deposits) in others. There is no fibrillary twitching; sensation is undisturbed; the electrical excitability of the muscles is de-

pressed; but there is no DeR (or rarely a slight DeR) in affected muscles. The development of the disease is slow. The patients exhibit a characteristic mode of rising from the recumbent position (climbing up the legs). Lordosis of the lumbar spine, a waddling gait, a "wasp waist," "loose shoulders" (the child "slipping through" when one places his hands

Fig. 600.—Progressive Muscular Dystrophy. The Child "Slips Through His Shoulders." (Med. Service, J. H. H.)

Fig. 601.—Two Brothers Showing Marked Muscular Dystrophy. (Courtesy of Dr. H. M. Thomas.)

under the child's arms and tries to lift him), a lagophthalmus, and the myopathic face (sphinxlike mask, transverse smile), are among the symptoms that may be observable. The course of the disease is long drawn out. Several varieties are distinguishable.

### i. The Facioscapulohumeral Type of Primary Myopathy

*(Landouzy-Déjerine type of progressive Atrophic Myopathy; Atrophic myopathy; Atrophie musculaire progressive de l'enfance of Duchenne de Boulogne)*

The atrophy begins in the muscles of the face, often existing there for a considerable time before involvement of the trunk. The disease begins in infancy. After a certain development has been reached the child exhibits the so-called *myopathic face* (Landouzy and Déjerine), in which there is an apathetic, indifferent look, the eyes are wide apart, the forehead is not wrinkled, the nasolabial folds disappear, and the lips become large, the upper lip often projecting (*tapir lip*). At first sight the face may suggest imbecility, but one soon sees that the mentality is not involved. On laughing, the patient is unable to elevate the angles of the mouth, so that the so-called *transverse smile* results. Whistling and puckering of the lips are no longer possible, and the child cannot pronounce the labial letters. The eyes cannot be completely closed, even in sleep. The development of the malady is very slow.

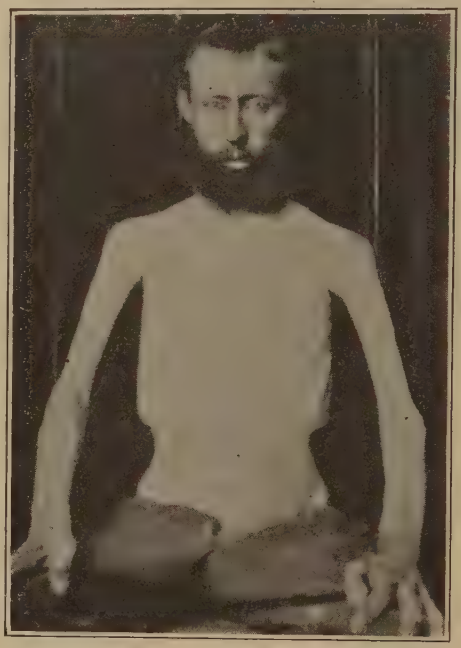

Fig. 602.—Case of Muscular Dystrophy of the Facioscapulohumeral Type, Showing Clearly the Thoracic Deformity Described by Marie as the "Wasp-shape"—"Taille de guêpe." (After P. Marie, "Exposé des Titres et Travaux Scientifiques," published by Masson & Co., Paris.)

The muscular atrophy may remain limited to the face, but, as a rule, it extends to the muscles about the shoulders, the two sides of the body being symmetrically involved. Here, the deltoid and the pectoral muscles become affected first and to the largest extent; later on, the muscles of the upper arm may atrophy. It is only very late in the disease if at all that the muscles of the forearm become involved.

The M. serratus magnus, the M. trapezius and the Mm. rhomboidei are early affected. The winged-scapulae (*scapulae alatae*) so common in this disease, are due to atrophy of the rhomboids.

The muscles of the lower extremity may be involved simultaneously with, or, as is more usual, later than, the muscles of the upper extremity. Here also the atrophy begins in the proximal muscles and extends only gradually to the more distal muscles of the extremities.

The muscles of the trunk, including the abdominal muscles and the muscles adjacent to the spine, are often early involved, giving rise to the *lordosis* of the disease. It is the atrophy of the trunk-muscles that compels these patients to climb up their legs when trying to stand up after lying recumbent.

The muscles of respiration, phonation, mastication and deglutition, as well as the eye-muscles, are not involved in this disease, except very rarely.

There is, as a rule, no hypertrophy or pseudohypertrophy of the muscles in this type of atrophy, if we except the formation of *muscle-balls* in the middle of some of the muscles, such as the deltoids and biceps.

The so-called *wasp-waist* of Marie is met with in this type. In this peculiar deformation of the thorax, the lower ribs are vertical, so that the waist is contracted at this level.

Another form of deformation of the thorax is also met with in this type. There is depression of the sternum and of the adjoining portions of the ribs (Landouzy and Déjerine).

### ii. The Scapulohumeral Type or Juvenile Form of Erb

In the facioscapulohumeral type described above, the face is usually involved first, though sometimes the shoulders and extremities are involved before the face.

A form of myopathy in which the face remains permanently intact, despite the scapulohumeral atrophy, has been described by Erb as the "juvenile form."

### iii. The Pseudohypertrophic Paralysis of Duchenne

*Pseudohypertrophic muscular paralysis; Dystrophia muscularis progressiva pseudohypertrophica infantum of Erb*)

In this form of myopathy, certain muscles are enlarged throughout their whole extent. The disease begins most often in early childhood, more rarely during adolescence. It occurs in families, though boys are more often affected than girls. The calves, hips and buttocks look extraordinarily large, though the arm muscles and the trunk muscles may be of normal size. The muscles are firm to the touch and elastic, though later in the disease they become softer. The legs are weak, the child tires easily and often falls when attempting to walk. Lordosis may be pronounced. The proximal muscles of both upper and lower extremities are involved in the atrophic or pseudohypertrophic process. The child on rising from the recumbent position first turns on the side, then gets on its knees, supporting the trunk upon the ground by means of the hands, finally climbing gradually up its legs to the erect posture.

### iv. The Leyden-Moebius Type; The Zimmerlin Type of Primary Myopathy

This type is closely allied to the preceding form but differs from it in that there is no hypertrophy, or very little, though the atrophy begins in the lower extremities, involving first the proximal muscles before extending to the more distally-placed groups. When the arms become involved, the same topographical law is obeyed.

**Differential Diagnosis.**—We must distinguish the primary myopathies (1) from the *neuritic forms of muscular atrophy* (begin with pains, no pseudohypertrophy, family history negative, topography of atrophy, *steppage* gait, disturbance of sensibility, paralysis out of proportion to the atrophy); (2) from the *progressive (central) muscular atrophies* (small muscles of hands involved; DeR present; fibrillary twitchings; onset, as a rule, in later life; often some spastic symptoms present); (3) from *progression neural muscular atrophy* (peroneal muscles first involved; proxi-

mal muscles of extremities unaffected, at least at the beginning, disturbances of sensibility); (4) from *Friedreich's ataxia* (*q. v.*); (5) from *Thomsen's disease* (*q. v.*); (6) *from myasthenia gravis* (*q. v.*).

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## (b) *The Muscular Atrophies Due to Degenerations of the Lower Motor Neurons*

### *Progressive Neuropathic and Myelopathic Muscular Atrophy; Deuteropathic Muscular Atrophy*

Aside from the muscular atrophy that follows any peripheral neuritis (mononeuritis, polyneuritis), acute poliomyelitis, and syringomyelia, we have to consider here (i) the spinal form of progressive (central) muscular atrophy, (ii) the bulbar form of progressive (central) muscular atrophy, (iii) the spastic form of progressive (central) muscular atrophy, usually called amyotrophic lateral solerosis, and (iv) the progressive neural form of muscular atrophy. In i and in iii the so-called Aran-Duchenne type of atrophy is met with.

### i. The Spinal Form of Progressive (Central) Muscular Atrophy

### (*Aran-Duchenne Type*)

This disease begins, usually slowly, in middle life, with fibrillary twitchings in the small muscles of the hand (thenar and hypothenar muscles; Mm. interossei, Mm. lumbricales), giving rise to the so-called "simian hand." The atrophy then extends to the muscles of the arms, shoulders and back, but rarely to those of the lower extremities. Sometimes, muscles innervated by cerebral nerves (See Bulbar Paralysis), or

the diaphragm, become involved. There is no hypertrophy, or pseudohypertrophy. Electrical excitability is depressed; there is partial DeR. Sensory disturbances are entirely absent, or are slight. This is relatively a rare disease, if the cases of syringomyelia and of polyneuritis resembling it are excluded from the group.

The muscular atrophy that accompanies amyotrophic lateral sclerosis is nothing but the spinal form of progressive (central) muscular atrophy combined with lesions of the pyramidal tract (*vide infra*).

**Werdnig-Hoffmann Type.**—A remarkable form of hereditary, or familial, occurrence of the spinal form of progressive (central) muscular atrophy occurring in infants, has been described by several writers (Werdnig, Hoffmann, Bruns, Batten, Bruce and Thomson). Several children of the same family are affected in infancy. The disease comes on between the 6th and the 12th month of life. There is weakness and atrophy of the muscles of the thighs, pelvis and back, which, later on, extends to the other muscles of the trunk and to the muscles of the extremities. The atrophy may be invisible at first on account of the adiposity of the young children. There is, however, no pseudohypertrophy and no genuine hypertrophy. The reflexes tend to disappear and the muscles show partial DeR. There are no disturbances of sensibility. Kyphoscoliosis may be present. There is bilateral, symmetrical involvement of the muscles. Bulbar symptoms sometimes co-exist. Death occurs in from one to six years. At autopsy, degeneration of the anterior-horn cells has been found.

On account of its occurrence as a family disease, its beginning in infancy, and its involvement first of the muscles of the trunk and the proximal muscles of the extremities, it closely simulates the primary myopathies, but on account of the kind of atrophy that is present and the degeneration of the anterior-horn cells, it clearly stands even more closely to progressive (central) muscular atrophy of spinal origin (Oppenheim).

Such a form, transitional between the primary myopathies, on the one hand, and progressive (central) muscular atrophy on the other, makes many neurologists believe that these two groups are perhaps more closely related than we have hitherto been accustomed to think (H. M. Thomas).

**Differential Diagnosis.**—(1) From *poliomyelitis anterior acuta* (quick development, simultaneous involvment of larger number of muscles, paralysis followed by atrophy); (2) from *amyotrophic lateral sclerosis* (spastic phenomena); (3) from *syringomyelia* and *gliosis spinalis* (sensory and trophic disturbances); (4) from atrophies following nerve compression in *caries* of the cervical spine, in *pachymeningitis cervicalis hypertrophica,* and in cases of *cervical rib.*

### ii. The Bulbar Form of Progressive (Central) Muscular Atrophy

(*Progressive Bulbar Paralysis, Paralysis glossopharyngolabiea progressiva*)

This is rather a rare disease, depending upon slight degeneration of the lower motor neurons of Nn. XII, XI, X, IX, VIII, etc. It begins, as a rule, after the 50th year. The cause is unknown.

There is a slowly developing dysarthria, at first for the linguals (S, L, D, T, N), later for the labials (P, B, M, F, W, O, U). The dysarthria is associated with difficulty in swallowing, in chewing and in speaking. Atrophy and fibrillary twitching appear in the muscles of the lips, tongue, soft palate, pharynx and larynx, and in the masticatory muscles. The "spongy" tongue and the thin lips are characteristic. Partial DeR can be made out in the muscles affected. The change in the facial expression (open mouth, hanging lower lip, drooling) may become striking; the upper facial domain often escapes. Sensation is normal.

Fig. 603.—Atrophy of the Tongue in Progressive Bulbar Paralysis. (After H. Oppenheim, "Lehrb. d. Nervenkrankh.," published by S. Karger, Berlin.)

Bulbar paralysis is sometimes a part of a progressive spinal muscular atrophy, or of an amyotrophic lateral sclerosis.

**Differential Diagnosis.**—(1) From *myasthenia gravis,* or so-called asthenic bulbar paralysis (*q. v.*); (2) from *pseudobulbar paralysis* (*q. v.*); (3) from *compression bulbar paralysis* (*e. g.,* tumor); (4) from the *acute* (*apoplectic*) *bulbar paralysis* of atherosclerosis, due to hemorrhage or to softening.

### iii. The Spastic Form of Progressive (Central) Muscular Atrophy
### (*Amyotrophic Lateral Sclerosis of Charcot*)

This disease is accompanied by degeneration of both of the two superimposed motor-neuron systems (upper and lower) of the corticomuscular path. Both anatomically and clinically it is a combination of the spinal (and bulbar) forms of progressive (central) muscular atrophy (anterior-horn lesion), with spastic spinal paralysis (pyramidal-tract degeneration).

It develops slowly. Weakness, atrophy and fibrillary twitching appear in the muscles of the upper extremities; or the disease may begin with weakness and spasticity of the lower extremities. There is marked

exaggeration of the deep reflexes; only slight sensory disturbances, if any, and no sphincter disturbances, are manifest. Bulbar symptoms, if they occur, set in, usually, late in the disease. The average duration is two to four years. Autopsies reveal (1) degenerations of the anterior-horn cells, and (2) degenerations of the pyramidal tracts from the foot of the cerebral peduncle downward (the degeneration advancing, gradually, from below upward).

Fig. 604.—Young Boy with "Amyotrophie Charcot-Marie." Atrophy of the Muscles of the Legs and of the Feet (Foot Drop). Atrophy of the Small Muscles of the Hands. (After P. Marie, "Exposé des Titres et Travaux Scientifiques," published by Masson & Co., Paris.)

Some authors look upon progressive spinal muscular atrophy, true bulbar paralysis, primary lateral sclerosis, and amyotrophic lateral sclerosis, all as various manifestations of a single disease, which they designate as *progressive (central) muscular atrophy;* many facts favor this view (H. M. Thomas).

**Differential Diagnosis.**—(1) From *myelitis cervicalis* (marked sensory disturbances, sphincter disturbances, no extension of the degenerative atrophy to the lower extremities); (2) from *poliomyelitis anterior chronica* (*q. v.*); (3) from *gliosis cervicalis* (sooner or later, syringomyelic dissociation of sensation from involvement of the posterior horns, slower course); (4) from *multiple sclerosis* (cerebral symptoms, like optic atrophy, nystagmus, loss of abdominal reflexes, etc.).

### iv. Progressive Neural (Neurotic) Form of Muscular Atrophy

*(Peroneal Type of Progressive Muscular Atrophy, Charcot-Marie Type, Tooth's Type, Hypertrophic and Progressive Interstitial Neuritis of Infancy or Déjerine-Sottas Type.)*

Age at onset, 8 to 30, or in the Déjerine-Sottas type, in infancy; females sometimes affected, but males predominantly attacked. Onset insidious. The atrophy appears first in the peroneal muscles, the extensors of the toes and the small muscles of the foot; club-foot (pes equinus, or pes equinovarus) develops and the legs waste; later, there is involvement of the distal muscles of the upper

extremities, with claw-hand. The legs below the knees often waste markedly. The proximal muscles of the extremities and the muscles of the trunk are unaffected; occasionally, fibrillary twitching is seen. There is a depression of electrical excitability and sometimes partial DeR in the muscles affected. Other symptoms include (1) loss of knee-kicks, (2) pains and hyperesthesias, and (3) absence of pseudohypertrophy. The disease follows a very slow course. It occurs in families, and is, in some instances, seen in more than one generation.

This type of muscular atrophy is not, strictly speaking, a system disease, for the neuritic process involves both the motor and sensory nerves, and, also, the posterior funiculi of the cord.

If the disease is a neuritis, it does not properly come in the group in which we have placed it. Probably, the syndrome corresponds to no single pathological-anatomical entity, as autopsies have shown very different conditions of the muscles, nerves, and spinal cord in different cases.

Under this heading, belong (1) the type described by Tooth, (2) the Charcot-Marie type, and perhaps, (3) the Déjerine-Sottas type (*Névrite interstitielle hypertrophique et progressive de l'enfance*).

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### (c) *Primary Degenerations Affecting the Upper Motor Neurons (Pyramidal Tracts) Alone*

#### i. Primary Lateral Sclerosis, Causing "Genuine" Spastic Spinal Paralysis (*Erb-Charcot Disease*)

Whereas amyotrophic lateral sclerosis involves both of the two superimposed neuron systems of the corticomuscular conduction path, and the spinal and bulbar forms of progressive (central) muscular atrophy involve the lower motor neurons alone (or almost alone), in primary lateral sclerosis ("genuine" spastic spinal paralysis), there is sometimes an isolated (or almost isolated) disease of the upper motor neurons (pyramidal tracts). Anatomically pure cases are, however, rare.

**Symptoms.**—The symptoms are those that follow lesions of the upper motor neurons; there is a slowly developing spastic pseudoparesis of the legs, with extreme hypertony, and exaggeration of the deep reflexes, without marked muscular atrophy and without loss of strength; there is no DeR in the muscles. The muscular rigidity is so great and interferes so much with voluntary movements, that the condition (pseudoparesis) simulates a true paralysis. Later on, there is some real weakness of the muscles (leg-shorteners).

The patients complain of the tension and stiffness in the legs, noticing it, first, on dancing, skating, or hill-climbing. The Babinski-phenomenon and the tibial phenomenon are positive.

A pure spastic gait is characteristic. The legs are stiff, the feet stick to the floor, there is strong adductor-spasm of the thighs, so that the legs tend to cross (scissors-gate); the pelvis is raised at each step, and the leg seems to move as a whole, with but little bending at the ankle and knee; still, the steps are not markedly shortened as long as there is no real paresis. There are no sensory, pupillary, or sphincteric disturbances, at any rate at first, and the eye-grounds are normal.

This disease is sometimes unilateral (Spiller, Mills).

This "genuine" spastic spinal paralysis is *a family and hereditary form of spastic paraplegia* (Strümpell). Two main types of the disease have been described.

In the *first type* there is, at first, a pure spastic gait with hypertonic pseudoparesis of the lower extremities, due to pyramidal-tract lesion alone (Strümpell's type). The disease occurs in families, and is heredi-

tary. It affects men more often than women, usually beginning at the end of the second, or in the third, decade. It is progressive, but slowly so, lasting one, two, or several decades. The muscles of the arms may become involved late in the disease, when, also, slight disturbances of sensibility, with ataxia, due to slight involvement of the posterior funiculi may develop. Occasionally, there is spasm of the M. sphincter vesicae.

In the *second type* that has been described, the disease begins in advanced life, and progresses relatively rapidly. Here, not only is there a spastic gait, with spastic pseudoparesis of the legs, but the arm-movements and the movements innervated by the cerebral nerves also become affected; the face grows rigid; there is dysarthria and cramp of the muscles of the glottis. Finally, the lower motor neurons may become involved.

Obviously, the first type tends to resemble "combined sclerosis," and the second type tends to resemble "amyotrophic lateral sclerosis." The differentiation can, however, usually be made.

"Genuine" spastic spinal paralysis is an excessively rare disease. Most of the cases with this erroneous diagnosis, have been cases of multiple sclerosis. But the latter is not a family disease; it shows sudden exacerbations and remissions; it is usually accompanied by visual and cerebral symptoms; there is weakness of the muscles as well as spasticity; the adductor-spasm in the thighs is rarely so marked at the beginning; ataxia, disturbances of sensibility, or intention-tremor, may be present; and the abdominal reflexes are often abolished.

**Differential Diagnosis of Primary Lateral Sclerosis.**—(1) From *multiple sclerosis, combined sclerosis,* and *amyotrophic lateral sclerosis* (*vide supra*); (2) from *myelitis* and *compression myelitis* (anamnesis, sensory and sphincteric disturbances); (3) from *hysterical paraparesis and contractures* (psychogenic factors, acute onset, non-organic contractures (*q. v.*), negative Babinski); (4) from *lues of thoracic cord* (arms free, Wassermann positive, therapeutic test).

### ii. Spastic Hemiplegia and Spastic Diplegia in Infants

(*Spastic Paralysis of Infants, Birth Palsies, Cerebral Palsies of Children, Little's Disease*)

We mention this condition here on account of its similarity, in some respects, to the spastic paralysis of adults, but it is probably never a primary degeneration of the pyramidal tracts, but always represents, either (1) a failure of the pyramidal tracts to develop, or (2) a secondary degeneration of the tracts, due to meningeal hemorrhage, or to encephalitis.

### iii. Spastic Paralysis Associated with Secondary Degeneration of the Pyramidal Tracts

Here belong the hemiplegias, paraplegias, etc., following cord-lesions of various sorts (myelitis, pernicious anemia, lues, cerebral lesions [hemorrhage, embolism, thrombosis, tumor], and cerebrospinal lesions [multiple sclerosis, lues.]).

The cases of *Erb's syphilitic spinal paralysis* probably belong here; but some of them may be true cases of primary lateral sclerosis, due to chronic intoxication in lues.

The so-called *hysterical spastic paraplegia* is not a true spastic condition at all, though pseudoclonus may be present. The Babinski-sign is negative.

For the other methods of differentiating organic from functional paralysis, see Disturbances of Motility.

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## 2. Primary Degenerations of the Sensory Neuron Systems

Certain parasites or their toxins appear to have an elective affinity for the intramedullary continuations of the axons of the peripheral sensory neurons, and for sensory neurons of higher orders. The most characteristic example is tabes dorsalis, in which the degeneration is almost limited to the sensory neuron systems. Subsequently, we shall discuss the degenerations in which the sensory symptoms are simultaneously involved with the motor systems (combined system diseases).

### (*a*) *Tabes dorsalis*

(*Posterior Sclerosis, Locomotor Ataxia, Parasyphilis of the Spinal Cord*)

On account of its frequency, course and duration, and the possibility of preventing it, this, for the general practitioner, is the most important disease of the spinal cord.

**Etiology.**—The disease is due to syphilis; either there is a low grade of luetic meningitis at the entrance of the posterior roots of the spinal nerves into the cord, causing compression and secondary degeneration, or there is a slow elective intoxication of the posterior funiculi resulting, in some way, from syphilitic infection. Men are affected three times as often as women. The age of onset is from 30 to 50, usually about 9–10 years after the primary luetic lesion. Children may have tabes (tabes infantilis, tabes juvenilis), due to hereditary lues. Over-exertion and exposure to cold are also important accessory etiological factors.

**Symptoms.**—No single sign is constant, but any two of the following symptoms and signs may be considered pathognomonic:

1. Lancinating pains in the lower extremities;
2. Loss of knee-kicks (Westphal's sign);
3. Pupils that react on accommodation, but not to light (Argyll-Robertson pupils);

4. Analgesia of the lateral surface of the legs, combined with tactile hypesthesia of the trunk;
5. Lymphocytosis in the cerebrospinal fluid with increase of globulin, and, in 50 per cent of the cases, a positive Wassermann reaction in the fluid. The gold-sol test in the fluid yields a characteristic curve.

Other early symptoms include:

6. Weakness of the bladder;
7. Paresthesias, girdle-feeling, feltlike feeling in soles of feet;
8. Optic atrophy;
9. Impotence;
10. Gastric and other crises (intestinal, laryngeal, renal, rectal);
11. "Rheumatic" pains in the joints;
12. Diplopia;
13. Romberg's sign (swaying with the eyes closed and feet together).

Later on, ataxia may develop (but only in about 30 per cent of the cases), involving the complicated movements of the upper and lower extremities, and giving rise to the typical ataxic gait (*q. v.*).

Trophic disturbances of the skin, bones and joints may develop (perforating ulcer of the foot, spontaneous fractures, tabetic arthropathies, falling out of the hair, teeth, nails, etc.).

Common complications include: (1) Luetic symptoms; (2) aortic insufficiency or aortic aneurism; (3) dementia paralytica.

**Pathological Anatomy and Pathogenesis.**—In the early stages, elective degenerations appear in the posterior funiculi of the spinal cord, corresponding to portions of the fibers from various posterior roots (neuralgic stage). Later on (ataxic stage), more extensive degenerations of the posterior funiculi are found, including the reflex collaterals and Clarke's columns. In the late stage (paralytic), there may be degenerations of the anterior horns, of the cells of Clarke's columns, and of the fibers of the direct cerebellar tract (so-called transneural degeneration, or extension of the degeneration beyond the limits of the neurons primarily affected). Optic atrophy is present in 10 per cent of the cases.

Various possibilities of the origin of tabes have been considered; some refer it to causes acting within the cord (endogenous origin), others to causes acting outside the cord (exogenous origin).

**Theories of Tabes.**—1. Some authors attribute the degeneration in the posterior funiculi to involvement of the posterior roots, by thickening of the pia (luetic inflammation), at their entrance into the spinal cord, thus making the disease meningitic in origin. Certainly, such a meningitis, due to the *Treponema pallidum,* may occur.

2. Others assume a primary disease of the spinal ganglia (trophic centers for the posterior roots), causing cellulipetal degeneration.

3. Still others see, in the tabetic process, a primary neuritis of the peripheral sensory nerves, which they hold responsible for a secondary degeneration of the spinal cord.

4. Another theory regards tabes as the result of a syphilitic disease of the lymph-vascular apparatus of the posterior funiculi, and of the meninges, corresponding to them.

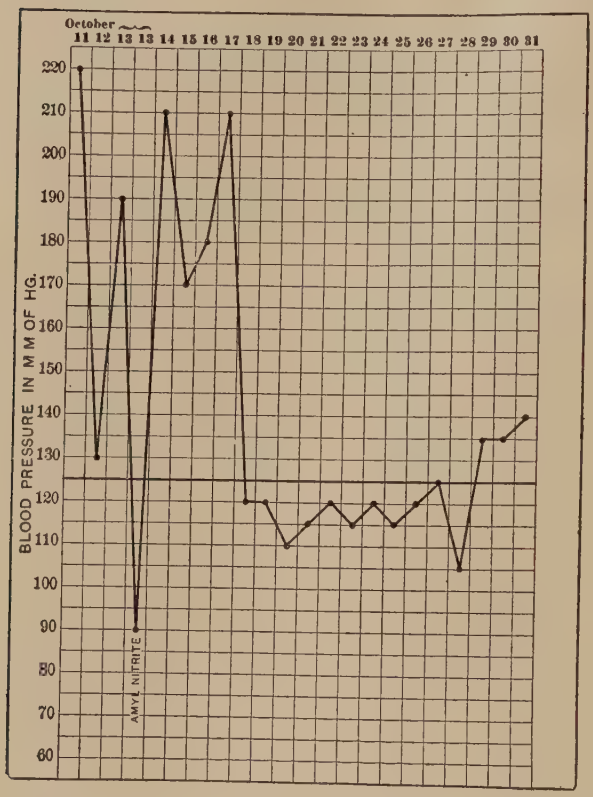


Fig. 605.—The Course of the Blood Pressure in Gastric Crisis in Tabes. (After L. F. Barker, Am. J. Med. Sci.)

5. Many favor the view that tabes is "a primary elective degeneration of the intramedullary continuations of the axons of the spinal-ganglion cells, picking out at first the shorter paths and those of medium length, and, later, involving other parts of the peripheral sensory neurons (long axons, spinal-ganglion cells, peripheral nerves)." It is possible, though not proved, that the noxa first injures the cell-bodies in the spinal ganglion, and that the first expression of this is a degeneration in the more distal parts of the central axon, which depends upon the cell for its nutrition.

**Differential Diagnosis.**—(1) From *polyneuritis* (etiology, quicker course, tenderness of muscles, anesthesias not segmental in topography, absence of Argyll-Robertson pupil and of sphincteric disturbances, lumbar puncture); (2) from *pseudotabes diabetica* (Wassermann reaction negative in both blood and cerebrospinal fluid, glycosuria, absence of Argyll-Robertson pupil and of bladder symptoms); (3) from *dementia paralytica* (*q. v.*); the two diseases are often combined (taboparesis).

### (*b*) *Other Primary Degenerations of the Sensory Neuron Systems*

Degenerations of the peripheral sensory neurons (posterior funiculi of the cord) are also met with in *ergotismus* (ergotin tabes) and in *pellagra;* as a rule, in pellagra, the lesions in the spinal cord are diffuse, and not systemic. In some of the cases of pseudotabes diabetica, the posterior funiculi are degenerated, though, more often, the symptoms in diabetes are due to a degeneration of the peripheral nerves.

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## 3. Combined Degenerations of Motor and Sensory Neuron Systems

Owing to the same cause, two or more neuron systems may simultaneously, or successively, degenerate. Here, as elsewhere, the separation of systemic and non-systemic diseases is difficult, since primary disseminated myelitic foci, causing secondary and retrograde degenerations, often give the impression of primary systemic diseases. For the present, we include, under the combined systemic diseases, certain syndromes in which the pathological lesions are at any rate *chiefly* confined to specific neuron systems. Under this heading, we shall discuss (1) Friedreich's disease, (2) hereditary cerebellar ataxia, (3) dementia paralytica, and (4) ataxic paraplegia.

### (*a*) *Familial Spinocerebellar Ataxia*

*(Friedreich's Disease, Hereditary Ataxia)*

This is a rare family disease, the onset, in affected persons, occurring in late childhood. Several children in one family are usually affected. The onset is slow with both locomotor and static ataxia (hence partly of tabetic, partly of cerebellar type; *démarche tabéto-cérébelleuse*). The deep reflexes are gradually lost (though the Babinski sign is sometimes positive). Speech disturbances may be prominent (slowing, in-

distinctness); nystagmus is common, also choreiform twitchings. Sensation is, usually, almost normal (no anesthesias nor lancinating pains). The pupils and the sphincters are normal. No paralysis or muscular atrophy can be made out. The psyche is usually normal. Scoliosis, kyphosis, and club foot are common. The disease is of long duration (20–30 years).

**Pathological Anatomy.**—There is a congenitally small spinal cord and medulla; combined degeneration of the posterior funiculi (especially of the funiculus gracilis) and of the lateral funiculi (pyramidal tracts; direct cerebellar tracts; Gowers' tract) are found. The ataxia is due to the degeneration of the spinocerebellar paths, the nystagmus and the dysarthria to degenerations in the brain-stem, and the loss of the deep reflexes to degenerations of the lower sensory neurons.

**Differential Diagnosis.**—(1) From *multiple sclerosis* in children (ataxia late, and, when present, combined with spastic paresis, exaggerated reflexes, and optic atrophy); (2) from *cerebral palsies of children* (*q. v.*); (3) from *congenital cerebrospinal lues* (more acute onset; oscillation of symptoms; cerebral-nerve involvement; spasticity; Wassermann test); (4) from *hereditary cerebellar ataxia* (*q. v.*).

Fig. 606.—Case of Hereditary Cerebellar Ataxia (Hérédo-ataxic Cérébelleuse) Photographed While Walking. (After P. Marie, "Exposé des Titres et Travaux Scientifiques," published by Masson & Co., Paris.)

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### (*b*) *Hereditary Cerebellar Ataxia* (*Marie; Sanger Brown*)

This disease is closely related to the preceding one, but deserves a separate nosological position.

**Symptoms.**—Onset after the twentieth year. The ataxia is usually of the pure cerebellar type, though, occasionally, it is combined with move-

ment ataxia and with intention tremor; the tendon reflexes are normal, or increased; eye-muscle paralyses (especially ptosis and abducens paralysis) are common; occasionally, there may be optic atrophy, and, sometimes, dysphagia. Scoliosis and other deformities are not a feature.

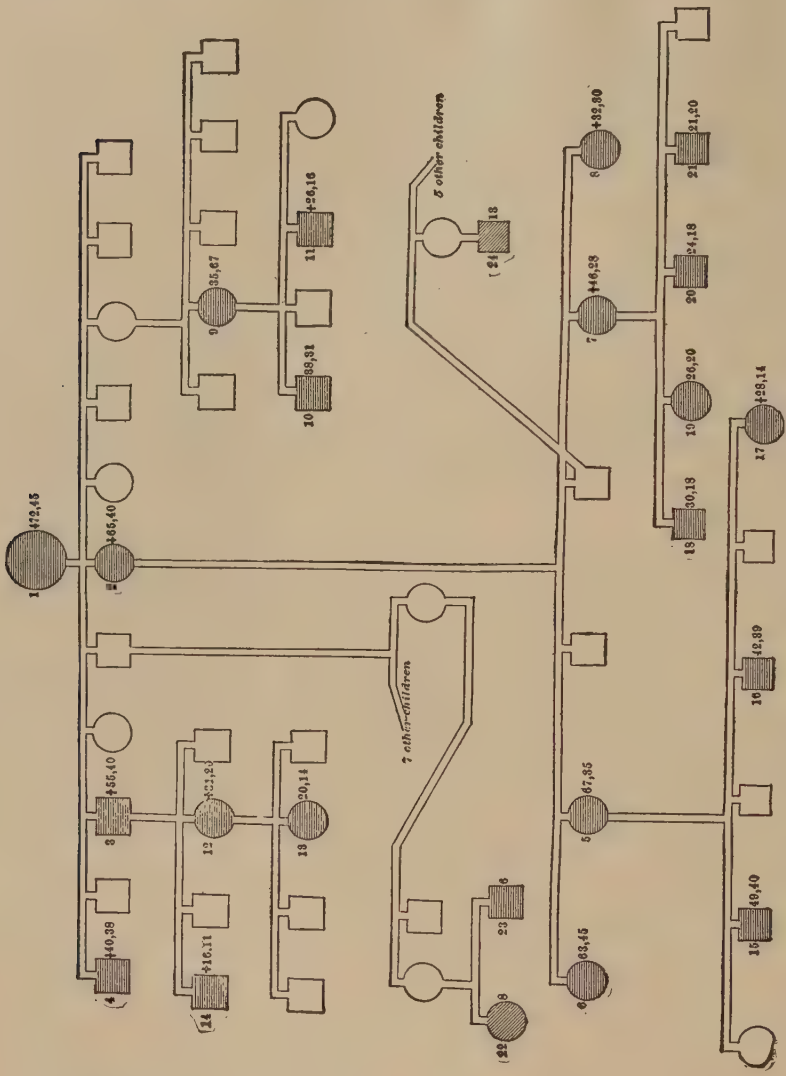
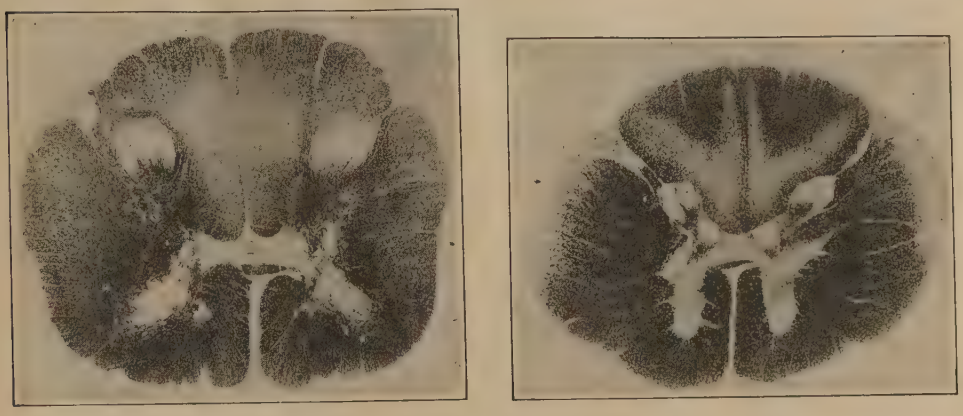



Fig. 607.—Family Tree of Hereditary Ataxia. (After Sanger Brown in L. F. Barker's Article in Decennial Publications, University of Chicago.)

**Pathological Anatomy.**—My own studies of the nervous system in Sanger Brown's cases revealed congenital hypoplasia of the cerebellum and of the spinal cord, with outspoken degenerations of the spinocerebellar paths (posterior funiculi; direct cerebellar tract; Gowers' tract), as well as slight degeneration of the pyramidal tracts.

It is possible that this hereditary cerebellar ataxia and Friedreich's disease together represent a single disease; in the one case, the cerebellar



A B

Fig. 608.—Lesions in the Cord in Hereditary Ataxia. Personal Observation. (Decennial Publications, University of Chicago.)

involvement predominating; in the other, the involvement of the spinal cord.

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## (c) *Dementia paralytica*

*(General Paresis, Progressive General Paralysis of the Insane)*

**Pathological Anatomy.**—Though elective sensory and motor degenerations do occur in this disease, we know now that patches of paraluetic encephalitis occur in it, due to the localization of the *Treponema pallidum* in the cerebral tissue (Noguchi and Moore). It might perhaps be more properly classified as a meningo-encephalitis and be placed under the inflammations of the nervous system. The lesions are chiefly in the brain, but the lower parts of the central nervous system, including the

spinal cord, to a certain extent, participate. In the brain, there is extensive atrophy and degeneration of the cortex, and, especially, loss of the fine medullated, tangential fibers in the superficial cortex, most marked in the frontal lobe and in the island of Reil. We include it here, among the combined systemic diseases, on account of the simultaneous involvement of the sensory neuron systems, the pyramidal tracts and the associative neurons. But the disease is, in reality, no respecter of systems!

**Etiology.**—The disease is always preceded by lues (congenital or acquired); the *Treponema pallidum* can be demonstrated in the cerebral

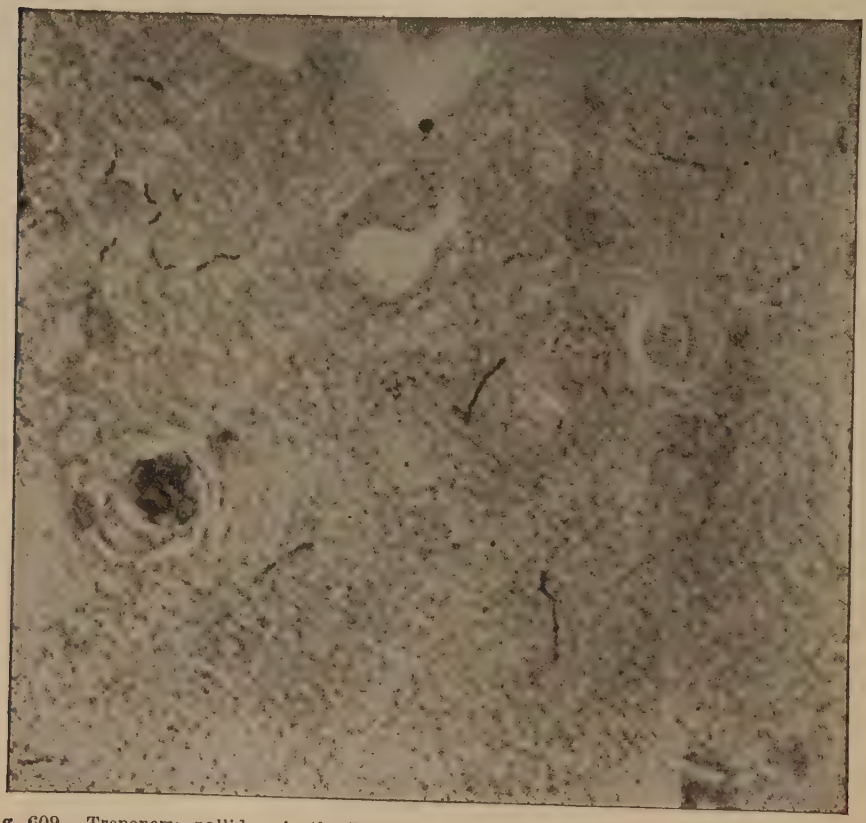

Fig. 609.—Treponema pallidum in the Brain in Dementia paralytica. (After H. Noguchi and J. W. Moore, studies from Rockefeller Inst. for Med. Research.)

lesions. The patient's blood and cerebrospinal fluid yield a positive Wassermann reaction; the cell count in the cerebrospinal fluid is high (lymphocytosis), and the gold-sol test yields a characteristic "paretic curve."

**Symptoms.**—These are partly *somatic,* including (1) Argyll-Robertson pupils, (2) anisocoria, (3) paralytic attacks (either apoplectiform or epileptiform), (4) speech disturbances in the form of syllable stum-

bling, and (5) changes in the reflexes; and partly *psychic,* including (1) progressive mental deterioration, manifested in ethical decline, (2) defective recording faculty, (3) loss of power of judgment, (4) defective memory, especially for recent events, (5) inability to concentrate attention, (6) abnormal irritability, and (7) mistakes in calculation; later, there may be (8) delusions of grandeur, or (9) hypochondriacal ideas, and sometimes (10) maniacal outbreaks. The patient has no disease insight, as a rule.

Death usually occurs within two or three years (infection, inanition, pneumonia). In taboparalysis, the duration may be very much longer, and the tabetic signs may predominate over those of dementia.

**Differential Diagnosis.**—1. In the initial stage from *neurasthenia* (absence of pupillary anomalies, of disturbed reflexes, and of speech disturbances; cerebrospinal fluid normal; exact psychic examination important).

2. From simple *tabes dorsalis with neurasthenia* (character of psychic disturbances; absence of motor lesions).

3. From *multiple sclerosis* (tremor constant, and strictly intentional; speech scanning rather than syllable stumbling; psychic involvement usually slight; cerebrospinal fluid normal).

4. From *lues cerebri* (headache; signs of focal lesions; absence of syllable stumbling; choked disk, rather than optic atrophy; absence of characteristic psychic disturbances).

5. From *tumor cerebri,* especially of the frontal lobe or of the region of third ventricle (choked disk; clouding of consciousness rather than true dementia; paralysis more permanent after attacks; absence of pathognomonic speech disturbances; no lymphocytosis in cerebrospinal fluid [Caution!]; Wassermann reaction negative).

6. From *cerebral atherosclerosis* and *senile dementia* (focal lesions with permanent hemiplegia, dysarthria, etc.; less dementia; disease insight usually present; cerebrospinal fluid normal).

7. From *chronic alcoholism* (delirium tremens; absence of Argyll-Robertson pupil; no lymphocytosis on lumbar puncture).

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### (*d*) *Combined Sclerosis of the Posterior and the Lateral Funiculi*

(*Ataxic Paraplegia* [*Gowers*], *Subacute Ataxic Paraplegia* [*Russell, Batten and Collier*]; *Primary Combined Sclerosis* [*Putnam*])

Here we have simultaneous, or successive, degeneration of the posterior and lateral funiculi; in the degeneration, the gracile and cuneate fasciculi, the pyramidal tracts, and the direct cerebellar tracts participate. The disease appears to be sometimes directly systemic, more often not; but it is, clinically, well characterized.

**Etiology.**—The affection is relatively common, though it varies in severity, in the severe anemias, especially in pernicious anemia; it is met with also in cachexias, after infections, and in chronic alcoholism.

In the cases associated with anemia, the symptoms referable to the spinal cord may follow, or may precede, the symptoms of anemia.

**Symptoms.**—The symptoms are a combination of (a) those due to degeneration of the posterior funiculi (as in tabes) with (b) those due to degeneration of the pyramidal tracts (as in spastic spinal paralysis). According as the degeneration affects the posterior funiculi more, or the lateral funiculi more, do the ataxic, or the spastic, symptoms, respectively, predominate. Of the symptoms due to degeneration of the posterior funiculi may be mentioned; (1) muscular hypotony; (2) loss of knee-jerks; (3) ataxia. Of the symptoms caused by degeneration of the pyramidal tracts may be mentioned; (1) muscular hypertony; (2) exaggeration of the deep reflexes, with positive Babinski; (3) motor weakness (paresis). Obviously, the one set of symptoms tends, more or less, to counteract the other. The spastic-ataxic gait is the most prominent symptom in all cases. Tingling, or numbness, of the fingers and toes is a common subjective complaint, sometimes the first symptom.

It is convenient to divide the cases into two groups, according as the posterior funiculi, or the lateral funiculi, respectively, are the more involved: Thus in one group, we have the syndrome of spastic spinal paralysis, to which are added ataxia, bladder weakness, lancinating pains, and other tabetic symptoms; and in the other group, we have the syndrome of tabes, to which is added motor weakness (paraparesis), with positive Babinski.

**Differential Diagnosis.**—1. From *tabes* and *dementia paralytica* (*q. v.*).

2. From *multiple sclerosis* (scanning speech; partial optic atrophy).

3. From *lues cerebrospinalis* (oscillation of the symptoms; Wassermann test; lumbar puncture).

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[Note.—See also references under the anaemias.]

### (e) *Degeneration of the Peripheral Motor and Sensory Neurons in So-called Neuritis*

What is ordinarily called neuritis is usually less an inflammation of the nerves than a primary degeneration, due to metabolic intoxication (diabetes, uremia, carcinoma, anemia), to exogenous poisoning (alcohol, lead, arsenic, etc.), or to infections (diphtheria, typhoid, tuberculosis, sepsis, etc.).

As a rule, local injuries, like pressure or trauma, cause a mononeuritis, whereas toxic and infectious agents give rise to a polyneuritis (multiple neuritis).

#### i. Mononeuritis

The symptoms will depend upon the nerve affected (See Topical Diagnosis).

#### ii. Polyneuritis (or Multiple Neuritis)

The symptoms vary somewhat according to the etiology.

##### (1) *Polyneuritis of Alcoholic Origin (Polyneuritis alcoholica)*

The onset is acute, or subacute, with paresthesias, and pains and weakness in the muscles of the extremities, leading to atonic muscular atrophy, with DeR. The nerves are tender on pressure. The tendon reflexes are

lost or diminished, except at the very beginning, when they may be exaggerated. Some nerves (Nn. peronei, Nn. tibiales postici, or Nn. femorales) are more often affected than others.

The topography of the paralyses and the anesthesias occurring as a result of the neuritis are not segmental in type, but correspond to the areas of distribution (motor and sensory) of peripheral nerves. The arms may not be affected at all, though, sometimes, there is a partial lesion of the N. radialis (the M. supinator, the M. brachioradialis and, often, the M. adductor hallucis longus, escaping). In both the arms and the legs, it is the distal, rather than the proximal, muscles that are paralyzed; the anesthesias, also affect the distal portion of the extremities, rather than the proximal. Ataxia often accompanies the motor weakness, and may be extreme (anesthetic form). The sensory symptoms are usually less marked than the motor; the combination of tactile anesthesia with hyperalgesia, especially of the soles of the feet, is characteristic, and almost pathognomonic. As a rule, there are no sphincter disturbances. Sometimes, marked psychic symptoms develop; the patients show a disorientation as regards time, place, and persons, and suffer from pseudoreminiscences—the so-called Korsakoff's or polyneuritic psychosis.

Fig. 610.—Alcoholic Neuritis. Wrist Drop and Foot Drop. Cirrhosis of Liver. Ascites, Korsakow's Syndrome. (Med. Service J. H. H.)

The cerebral nerves are sometimes involved (ophthalmoplegias; optic neuritis with central scotoma; vagal symptoms).

The symptoms of polyneuritis develop acutely or subacutely, reaching a maximum in a few weeks, or months, after onset. Very acute cases yield the picture of Landry's paralysis (*q. v.*). Recurring forms are sometimes met with.

Convalescence is slow, the neuralgias and the tenderness to pressure disappearing first, the hyperalgesia and the paralyses persisting longer.

The extent to which recovery may go is marvellous, considering the severity of the symptoms, though a few muscles may remain permanently paralyzed, with development of contractures in their antagonists.

### (2) *Polyneuritis Due to Lead Poisoning*
### (*Polyneuritis saturnina*)

In lead poisoning, the N. radialis is most often degenerated; sometimes the N. medianus and the N. ulnaris are also involved. The degen-

Fig. 611.—Lead Line in the Gums in Histological Section. Note the Deposits (b) of Lead Sulphid in the Connective Tissue of the Papillae. (After H. M. Thomas, J. H. H. Bull.)

eration affects especially the terminals of the nerves rather than the large trunks. Only motor fibers are attacked. It is a *pure motor neuritis*, with paralysis; there is no disturbance of cutaneous sensibility. The anterior-horn cells show changes.

Lead miners, typesetters, painters, plumbers, tinsmiths and battery makers are chiefly affected. Chronic lead poisoning may also occur in actors from cosmetics used in the make up (personal observation).

The paralysis usually affects both arms, involving first the extensors of the hands and fingers (*wrist drop*). Of the muscles innervated by the

N. radialis, the M. brachioradialis and the M. triceps escape. Occasionally, lead palsy involves the cords of the brachial plexus, causing either an upper paralysis of Remak's type, or a lower paralysis of Klumpke's type (*q. v.*). The fibrillary twitching, often present in the paralyzed muscles, suggests an action of the lead directly upon the cell-bodies in the anterior horns.

When the leg is affected, the paralysis is in the domain of the N. peroneus, though the M. tibialis anterior escapes.

The localization of the paralyses in lead poisoning gives, as a rule, the clue to the etiology; examination usually reveals other signs of lead poisoning (dark blue line on gums; basophile Grawitz granules in the red blood corpuscles; tremor saturninus; lead colic; arthralgias; etc.). Chronic lead poisoning may be complicated by anemia, atherosclerosis, gout, or chronic nephritis.

### (3) *Polyneuritis Due to Arsenical Poisoning*

### (*Polyneuritis arsenicosa*)

This, when acute or subacute, most often follows attempts at suicide, though sometimes it results from injudicious arsenical medication. Chronic arsenical poisoning may come from wall paper, carpets, beer, etc. The polyneuritis is usually preceded by gastro-intestinal disturbances.

**Symptoms.**—The patients complain of pains and anesthesias in the distal portions of the extremities; these are soon followed by atrophic paralyses, with DeR. Both the extensor and the flexor muscles are involved in all four extremities (tetraplegia, chiropodal paralysis). Objective hypesthesias can be demonstrated; ataxia is common; the knee-jerks are lost; atrophic disturbances in the skin are frequent (pigmentation, herpes, pemphigus, hyperkeratosis, etc.). The cerebral nerves are not involved. Psychic disturbances sometimes develop.

### (4) *Polyneuritis Due to Beriberi*

The noxa of the disease (lack of a vitamine in the diet) causes endoneural proliferation and degeneration of the nerve fibers, especially in the N. tibialis, N. peroneus, N. vagus, N. phrenicus and N. splanchnicus. The involvement of the cardiac fibers (palpitation, anginal pains, disturbance of rhythm), and of the vasomotor nerves (edemas) is characteristic. In the "dry form," there are extensive atrophies, with DeR. in the muscles of the legs. The condition has been carefully studied by K. Miura. See Part XIII.

### (5) *Polyneuritis Complicating Diphtheria* (*Polyneuritis diphtherica*)

This is the commonest form of neuritis complicating an infectious process. Whether it depends upon an ascending peripheral neuritis from the local infection, or intoxication, in the throat, involving the motor cerebral nerves (Nn. XII, X, IX, VII), or whether the nerves degenerate as a result of intoxication of the motor neurons as a whole from absorbed toxins, is not certain; the former seems more probable when the throat alone is involved, the latter when distant nerves degenerate.

**Symptoms.**—The paralyses occur, usually, two or three weeks after the diphtheria, manifesting themselves in nasal speech, dysphagia, and regurgitation of fluids through the nose; there is palatal paralysis and loss of the palatal reflex. Besides involvement of the laryngeal and pharyngeal muscles, the eye-muscles, especially the M. ciliaris (accommodation-paralysis) may be involved. Bradycardia, tachycardia and arhythmia may point either to involvement of the N. vagus, or to a complicating myocarditis. The knee-kicks and the ankle-jerks are often lost. In rare cases, the diphtheritic polyneuritis extends to the motor and sensory nerves of the extremities (paralyses, anesthesias, ataxia); the sphincters are usually normal.

### (6) *Polyneuritis of Unknown Infectious Origin* (*Polyneuritis infectiosa idiopathica*)

This begins with fever, pain in the head, limbs, and back, and, sometimes, delirium. The spleen is palpable. Albuminuria, vomiting, diarrhea, sometimes icterus, and profuse sweats may accompany the disease. Paralyses in various parts of the body, or ataxia, soon follow. The sensory nerves and the sphincters suffer less than the motor nerves. Korsakoff's psychosis (*q. v.*) may complicate the picture. The patients usually recover slowly, but death may occur from involvement of the N. phrenicus—respiratory failure—or of the N. vagus—heart failure (See Landry's paralysis).

### (7) *Other Forms of Polyneuritis*

Toxic polyneuritis may complicate tuberculosis, carcinoma, tabes, or diabetes. A multiple neuritis may also complicate influenza, lues, typhoid fever, leprosy, erysipelas, puerperal, and other septic infections. In intoxications with $CS_2$ and with CO polyneuritis may occur; in the latter, there are violent initial symptoms on the part of the cerebrum (convulsions, coma). Alimentary toxemia is a frequent cause of polyneuritis (von Noorden).

**Differential Diagnosis of Polyneuritis.**—The topography of the paralyses or anesthesias, the acute development of the symptoms, the toxic

or infectious etiology, the non-involvement of the bladder, rectum and pupils, usually make the diagnosis easy. In special cases, polyneuritis must be differentiated:

1. From *tabes dorsalis* (segmental topography of the anesthesias, pupils, cerebrospinal fluid);
2. From *dementia paralytica* and other diseases causing mental disturbances (when Korsakoff's psychosis complicates the polyneuritis);
3. From *poliomyelitis anterior acuta* (topography of symptoms, mode of onset and spread, rare involvement of cerebral nerves);
4. From *trichinosis* (eosinophilia, edema of the eyes, histology of excised or harpooned muscle).

It should be kept in mind that the same patient may have several attacks of polyneuritis—so-called "recurring multiple neuritis" (Mary Sherwood).

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# E. Diseases of the Nervous System Due to Inflammatory Processes

Under this heading we include (1) diseases due to acute and chronic inflammations of various sorts, and (2) the diseases due to certain specific inflammations (the infectious granulomata).

## 1. Diseases of the Nervous System Due to Acute and Chronic Inflammations

These include the different forms of encephalitis, myelitis, and meningitis. Under this heading we include also multiple sclerosis, though whether it should be designated an inflammatory process is doubtful.

### (*a*) *The Different Forms of Encephalitis*

Encephalitis may be (i) *purulent* (encephalitis purulenta, or abscess of the brain), or (ii) *non-purulent* including (1) acute hemorrhagic encephalitis (2) poliencephalitis hemorrhagia superior acuta and (3) the forms of encephalitis that give rise to the cerebral palsies of children.

#### i. Purulent Encephalitis

(*Abscesses of the Brain, Encephalitis purulenta*)

Abscess of the brain is due to infection with pyogenic bacteria (streptococci, staphylococci, pneumococci, etc.). Most frequently, it arises from extension of local disease (otitis, mastoiditis, paranasal sinusitis, trauma); sometimes, by hematogenous metastasis (pyemia, pneumonia, empyema, bronchiectasis, etc.).

**Symptoms.**—These may appear suddenly, or develop slowly, after a latent period. The symptoms vary, according as the origin is traumatic, otitic, or metastatic. *Traumatic abscesses* usually have an acute onset and cause symptoms like those of purulent meningitis; *otitic abscesses* may develop slowly and cause symptoms and signs resembling those of tumor cerebri, including, (1) symptoms of increased intracranial pressure (headache, vertigo, bradycardia, vomiting, convulsions, though not always choked disk), and (2) focal symptoms referable to the left temporal lobe (sensory aphasia). Larger abscesses of the temporal lobe may cause neighborhood symptoms (hemiparesis, hemi-anesthesia, hemi-anopsia,

conjugate deviation, aphasia), or symptoms referable to compression of the cerebral nerves at the base (ptosis, abducens paralysis).

*Metastatic abscesses* may give rise to focal symptoms, corresponding to their location; thus in the parietal and occipital lobe, hemianopsia; in the motor area, monoplegia; in the frontal lobe, motor aphasia; in the cerebellum, occipital neuralgia, rigidity of neck, vertigo, nystagmus, asynergy, cerebellar ataxia.

Fever and chills may occur, but the temperature may be normal, or even subnormal, especially in uncomplicated cases. There is usually some polymorphonuclear leukocytosis, revealed by the blood count.

**Differential Diagnosis.**—This may be extremely difficult, unless the etiology is clear. The diagnosis of the site of the abscess is most important for the surgeon (see Topical Diagnosis). In doubtful cases, we should always consider the possibility of confusion with (1) *tumor cerebri*, (2) severe *neurasthenic states*, (3) *sinus thrombosis*, (4) diffuse *purulent meningitis* (bradycardia, lumbar puncture), and (5) *meningitis serosa*.

For the diagnosis of cerebellar abscess, see Vestibular Syndromes.

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### ii. The Non-purulent Forms of Encephalitis

#### (1) *Acute Hemorrhagic Encephalitis*

*(Encephalitis hemorrhagica acuta, Acute Non-purulent Encephalitis, Strümpell-Leichtenstern Type of Encephalitis)*

This is an acute inflammation of the brain, with hemorrhagic exudate, which is often followed by focal softening, and, later, by cysts and porencephalic defects. The disease is due to the metastatic localization of some infectious agent in the brain; it is met with as a complication of influenza, scarlet fever, whooping-cough, acute articular rheumatism, typhoid fever, measles, pneumonia, ulcerative endocarditis, etc. In some cases, the meningococcus may be responsible; in some, also, the virus of the Heine-Medin disease.

**Symptoms.**—The onset is acute, with high fever, chill, and drowsiness, deepening into sopor or coma; often there is delirium; occasionally, convulsions. The focal symptoms vary according to the site of the inflammatory deposits (monoplegia, hemiplegia, aphasia, hemi-anopsia, hemi-ataxia, etc.).

**Differential Diagnosis.**—(1) From simple toxic *meningismus* (absence of definite focal symptoms); (2) from *sinus thrombosis* (*q. v.*); (3) from *meningitis serosa* (*q. v.*); and (4) from *tumor cerebri.*

#### (2) *Poliencephalitis hemorrhagica superior acuta*

*(Wernicke-Thomsen Type of Encephalitis, Acute Ophthalmoplegia)*

This is an acute hemorrhagic encephalitis, limited to the central gray matter in the floor of the third ventricle and around the aqueductus cerebri, though sometimes it extends into the floor of the fourth ventricle. The small hemorrhages overshadow the inflammatory exudate on post-mortem examination.

**Etiology.**—The disease is probably an infectious process; it is most frequently met with as a complication of chronic alcoholism.

**Symptoms.**—The onset is acute and the course rapid, the disease usually terminating fatally within a week or two; recovery is rare. There is no fever. The patients grow drowsy and delirious. Paralysis of the eye-muscles, usually total ophthalmoplegia, soon sets in; M. sphincter iridis and M. levator palpebrae superioris sometimes escape). This is due to the involvement of the nucleus N. oculomotorii, nucleus N. trochlearis, and nucleus N. abducentis in the lesion (*poliencephalitis superior*). The patients show an ataxia of the cerebellar type, due to involvement of the nucleus ruber and the brachium conjunctivum.

Sometimes the process extends to the motor nuclei of the cerebral nerves in the pons and in the medulla (*poliencephalitis inferior*), some-

times also to the anterior horns of the cord (*poliencephalomyelitis*). Some of the latter cases reported may have been instances of the Heine-Medin disease, causing acute ophthalmoplegia and acute bulbar paralysis in addition to the ordinary paralysis of the extremities from anterior-horn lesions.

**Differential Diagnosis.**—The diagnosis should be most carefully made (1) from the *ptomain paralyses in botulismus* (usually a bilateral ophthalmoplegia interna, etiology); (2) from *sleeping sickness* (trypanosomes in juice from cervical lymph glands); (3) from acute ophthalmoplegia due to *neuritis of the eye-muscle nerves;* and (4) from ophthalmoplegia due to *traumatic hemorrhage in the central gray matter.*

### (3) *The Cerebral Palsies of Children*

(*Encephalitis infantilis, Paralyses Due to Intrapartum Meningeal Hemorrhages* [*Cushing*], *Hemiplegia spastica infantilis, Diplegia spastica infantilis*)

In intra-uterine or in early extra-uterine life various lesions occur, which may give rise to hemiplegia, diplegia, arrested development, etc. Forceps delivery may cause meningeal hemorrhage (Cushing); infectious diseases (measles, scarlet fever, Heine-Medin disease, whooping-cough, endocarditis, etc.) may cause hemorrhagic encephalitis, or lead to cerebral embolism or thrombosis.

As results of these processes there is softening, cyst formation, and, later, induration, or sometimes a *porencephaly,* the defect being in the form of a hole in, or funnel-shaped retraction of, the cortex, often extending to the ventricle; or there may result either a general sclerosis, or a local (lobar) sclerosis. The motor areas of the cortex (domain of middle cerebral artery) are most often affected, and these lesions give rise to the "cerebral palsies of children."

**Symptoms.**—The cases due to injury at birth may occasionally be observed in the initial stage; there are fever, vomiting, delirium, drowsiness, and convulsions, followed by hemiplegia or diplegia. Usually, however, the physician sees only the after effects (residual hemiplegias, diplegias with contractures, and often with imbecility, or epilepsy). Hemi-athetosis, hemichorea, and speech disturbances are common. The patients with diplegia show marked acusticomotor reactions on hearing noises (Oppenheim). Various attempts have been made to subdivide the cerebral palsies into groups (see Osler's Monograph). Among these may be mentioned: (1) *Little's disease* (congenital spastic rigidity of the limbs, walking learned late, gait spastic, with exaggerated reflexes, often associated with strabismus, indistinctness of speech, feeble-mindedness, epilepsy, choreiform, or athetotic, movements); (2) *paraplegic rigidity;* (3) *bilateral hemiplegia;* (4) *double congenital athetosis* with rigidity, in

which there are remarkable pathological associated movements (*q. v.*); the mind may be intact; (5) *amaurotic family idiocy* (Sachs); in which certain Jewish children, besides idiocy, exhibit a tetraplegia, optic atrophy, nystagmus, and typical macular changes on ophthalmoscopic examination.

**Differential Diagnosis.**—Usually easy (1) from spinal *poliomyelitis anterior* (signs of lower-motor, not of upper-motor neuron lesion; non-involvement of the face; absence of athetosis); (2) from *Sydenham's chorea* (age, duration, co-existence with tonsillitis or endocarditis, etc.); (3) from *idiopathic epilepsy* (anamnesis, absence of spasticity); (4) from *hysteria* (I have seen one case of *athétose double* in which the diagnosis of hysteria had been made).

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### (b) *The Different Forms of Myelitis*

This term is used to include the degenerative, circulatory (exudative and infiltrative) and productive changes in the nerve cells, nerve fibers and neuroglia of the spinal cord. Very often, pathologically, we have to deal with softening, or necrosis, from arterial thrombosis.

Clinically, we subdivide the cases of myelitis into (a) myelitis, involving both white and gray matter, and (2) poliomyelitis involving the gray matter only.

#### i. Myelitis Involving both the White and the Gray Matter

This may occupy different parts of the cross-section at a given level [myelitis transversa, centralis, disseminata, peripherica (meningomyelitis)]. The part of the cord involved may also give the name to the process (myelitis cervicalis, thoracalis, lumbalis and sacralis).

**Etiology.**—Myelitis follows infectious, or toxic, injuries of the spinal cord; most often, perhaps, it is due to an infectious arteritis with throm-

bosis causing anemic necrosis, and occurring as a complication of measles, scarlet fever, typhoid, smallpox, gonorrhea, diphtheria, or sepsis. It occurs, also, after exposure to cold (beggars, winter campaigners). Luetic forms are described farther on.

**Symptoms.**—The motor, sensory, and reflex disturbances correspond to the part of the cord injured (See Topical Diagnosis).

### (*1*) *Myelitis cervicalis*

This may involve the *upper cervical cord,* in which event there is spastic (non-degenerative) paralysis of both arms and legs; anesthesia of the whole body below the neck; sometimes paralysis of the diaphragm; occasionally bulbar symptoms. Or it may involve the *cord at the level of the cervical enlargement.* This causes (1) atrophic paralysis of the upper extremities, with DeR in the paralyzed muscles; (2) loss of reflexes; (3) spastic (non-degenerative) paralysis of the lower extremities with increased reflexes and positive Babinski; (4) anesthesia below the neck; and (5) sometimes oculopupillary symptoms corresponding to involvement of $T_1$.

### (*2*) *Myelitis thoracalis*

This is the commonest form. The upper extremities are normal. There is spastic, non-degenerative, paralysis of both lower extremities; the Babinski sign is bilaterally positive. The lower extremities, and the lower part of the trunk up to some definite segmental level, are anesthetic.

### (*3*) *Myelitis lumbalis*

When the lesion is situated in the lumbar region, the upper extremities and the trunk are normal. There is flaccid, atrophic, paraplegia of the lower extremities with DeR; the knee-kicks are absent; there is anesthesia of the legs and of the trunk up to some point below the umbilicus.

### (*4*) *Myelitis sacralis*

In lesions of the pars sacralis, there is atrophic paralysis of the Mm. glutei, of the flexors of the knee, and of the muscles innervated by the N. peroneus. The riding-breeches anesthesia ($S_2$) is characteristic. The ankle-jerk and the plantar reflexes cannot be elicited.

In all forms of myelitis there are disturbances of the sphincters (incontinence), and, usually, certain trophic and vasomotor disturbances (tendency to decubitus; sometimes desquamation, edema or herpes).

The symptoms vary according to the completeness of the interruption of the conduction paths within the spinal cord. In partial transverse lesions, the sensory disturbances may be slight, especially at the onset.

If the myelitis affect one half of the spinal cord only, a Brown-Séquard syndrome (*q. v.*) develops.

### (5) *Myelitis disseminata*

In myelitis disseminata, there are multiple inflammatory foci in the most different parts of the spinal cord; often the pons, the medulla oblongata, the cerebellum, and the cerebrum are involved at the same time, in which event the condition is called encephalomyelitis disseminata. It is always infectious, or toxic, in origin.

The symptoms depend upon the situation, and the extent, of the several foci. In many cases, an optic neuritis (sometimes a retrobulbar neuritis) precedes the change in the spinal cord. Tremor, ataxia, scanning speech, and mental enfeeblement are prominent symptoms, which, were it not for their acute appearance, would suggest multiple sclerosis. Many cases of so-called "acute ataxia" belong here, though others are due to multiple neuritis.

Most cases of myelitis have an acute onset. One of my patients, apparently well before, felt his legs give way suddenly while playing a round of golf. Subacute and chronic cases are sometimes met with.

**Differential Diagnosis of Diffuse Myelitis.**— (1) From *multiple sclerosis* (*q. v.*); (2) from *tumor* of the spinal cord; (3) from *compression paralysis* due to vertebral disease; (4) from *myelomalacia,* due to embolism, or thrombosis, of the arteries supplying the spinal cord; (5) from *hysteria* (absence of sphincter disturbances; negative Babinski's sign; psychogenic factors).

Fig. 612. — A Case of Acute Poliomyelitis with Intercostal Paralysis, Showing Protrusion of the Abdomen by Contraction of the Diaphragm and Concomitant Retraction of the Thorax. (After F. W. Peabody, G. Draper and A. R. Dochez, Mon. of the Rockefeller Inst. for Med. Research.)

### (6) *Acute Ascending Paralysis*
### (*Paralysis ascendens acuta, Landry's Paralysis*)

This clinical syndrome (with varying anatomical basis), is characterized by a sudden flaccid paralysis of the legs, with loss of the tendon reflexes, followed, within a few days, by paralysis of the trunk and of the arms, and, later still, after extension of the lesions to the medulla oblongata, by paralysis of the lips, throat, and larynx (dysphagia, dysarthria). The malady often (not always) begins with fever and general

Fig. 613.—Photograph of a Case of Acute Poliomyelitis with Profound Stupor, Showing Irritated Expression. The Paralyzed Left Arm Has Been Flung Over by the Shrugging of the Shoulder. Retraction of the Neck. (After F. W. Peabody, G. Draper and A. R. Dochez, Mon. of the Rockefeller Inst. for Med. Research.)

malaise; there is tachypnea, and sometimes Cheyne-Stokes breathing. Some patients recover; the majority die in from seven to ten days, usually from asphyxia. The disturbances of sensibility are usually slight, and the sphincters are rarely disturbed.

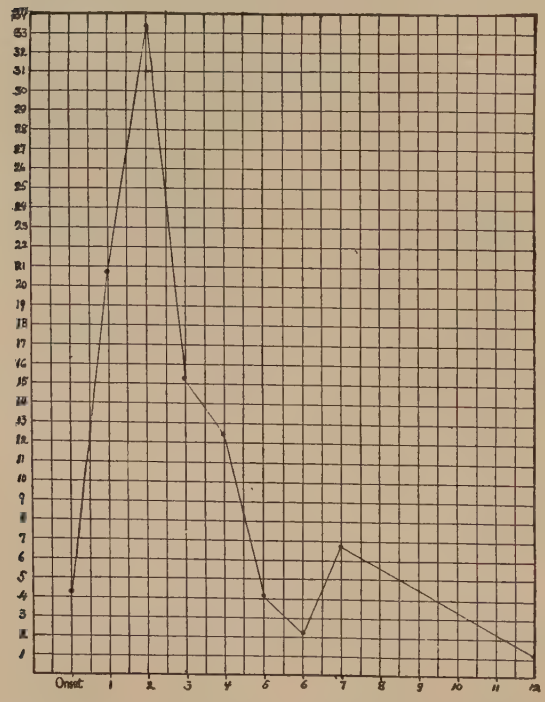


Fig. 614.—Acute Poliomyelitis. Chart Showing Relation of Onset of Paralysis to the Day of Disease. (After F. W. Peabody, G. Draper and A. R. Dochez, Mon. of the Rockefeller Inst. for Med. Research.)

**Pathogenesis.** — The condition is nearly always due to bacterial infection (*Bacillus typhosus, Bacillus anthrax, Staphylococci*), the toxins injuring especially the motor paths and not necessarily causing gross alterations in the tissues. The pathological findings vary (myelitis disseminata, poliomyelitis, polyneuritis). Writers have, accordingly, distinguished a spinal, a neural, and a bulbar type. In a few cases, the process begins in the medulla oblongata and descends (acute descending paralysis).

### (7) *Abscess of the Spinal Cord* (*Myelitis purulenta*)

Abscess of the spinal cord is extremely rare; when it occurs, it is either traumatic in origin, or metastatic (gonorrhea, cystic or prostatic infection, septic endocarditis, putrid bronchitis). The symptoms depend upon the level of the spinal cord affected, and are usually accompanied by radiating pains due to simultaneous involvement of the meninges.

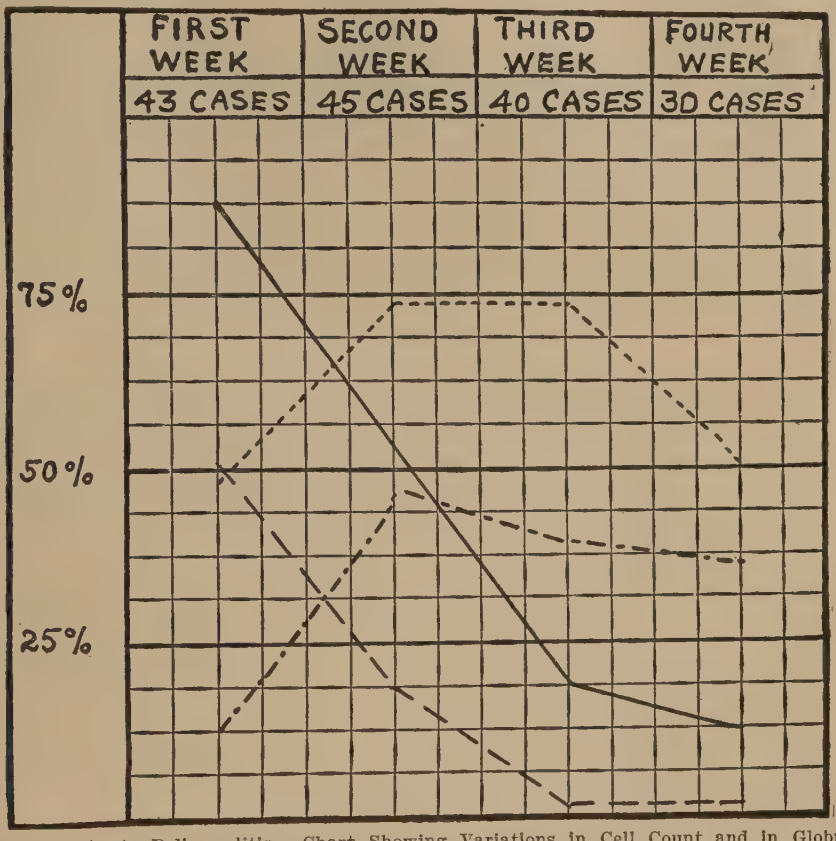


Fig. 615.—Acute Poliomyelitis. Chart Showing Variations in Cell Count and in Globulin Content of Cerebrospinal Fluid. ——— Percentage of Cases with Cell Count Above Normal. — — — Percentage of Cases with Cell Count Above 50 per c.mm. - - - - - Percentage of Cases with Globulin Slightly +. — - — - — - Percentage of Cases with Globulin + or over. (After F. W. Peabody, G. Draper and A. R. Dochez, Mon. of the Rockefeller Inst. for Med. Research.)

### ii. Acute Anterior Poliomyelitis

(*Poliomyelitis anterior acuta, Infantile Spinal Paralysis, Spinal Localization of the Heine-Medin Disease, Encephalomyelitis acuta infiltrativa*)

See The Heine-Medin disease, under Diagnosis of the Infectious Diseases.

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### (c) *Multiple Sclerosis*

*(Sclerosis multiplex cerebrospinalis, Nodular Sclerosis, Disseminated Sclerosis)*

We consider this here, though it is not certain that it is due to a chronic inflammation. It is essentially a disease of youth, beginning usually between the fifteenth and thirtieth years. Though I have seen a number of patients over 40 suffering from the disease, the anamnesis showed an onset a decade earlier. It is, unfortunately, a relatively common disease.

**Etiology.**—The cause is unknown, though the disseminated nodules have been seen to appear after various infections (typhoid, scarlet fever, whooping-cough, pneumonia, influenza), and intoxications (lead, zinc, copper).

**Symptoms.**—Owing to the fact that the peculiar nodules appear in the most different parts of the central nervous system, the symptomatology is extremely variable. The disease is, accordingly, often overlooked; it is the organic disease that is most often, perhaps, confused with hysteria.

The motor disturbances (paralyses) are usually more pronounced than the sensory. The other most characteristic symptoms are: (1) slow, indistinct, scanning speech; (2) intention tremor, especially in the upper extremities; (3) nystagmus. The motor symptoms may include spastic paresis, paraplegia, hemiplegia and epileptiform convulsions. Neuralgias, or anesthesias, may complicate the picture. In typical cases, the diagnosis is easy, but, more often, the disease begins with an obscure spastic paraparesis, the cerebral phenomena being at first slight or entirely absent. *Three very important symptoms for the early diagnosis are* (1) *loss of abdominal reflexes,* (2) *weakness of abdominal muscles, and* (3) *temporal pallor of the optic disks.*

Remarkable remissions and exacerbations occur in the course of the disease.

**Pathological Anatomy.**—Dozens, or even hundreds, of circumscribed nodules are distributed (according to no known law) through the central nervous system, and the symptoms are predominantly cerebral, bulbar, cerebellar, or spinal, according to the predominant localization within the central nervous system.

The nodules are circumscribed, gray or pink in color, and of variable consistence. There are certain sites of predilection (medulla and pons, corpus callosum, wall of lateral ventricle, cerebral peduncles; the white matter of the centrum semi-ovale and of the spinal cord). Nodules are seldom found in the cerebral cortex.

The myelin sheaths of the nerve fibers passing through the nodules are degenerated, but, strangely enough, the axons are, as a rule, preserved, and can still be stained (hence very little secondary degeneration). The glia undergoes proliferation in the nodules, especially around the blood vessels.

**Differential Diagnosis.**—Multiple sclerosis must be distinguished (1) from *hysteria* (absence of true spasticity and of Babinski phenomenon; no optic atrophy; abdominal reflexes present; no typical intention tremor; relation of symptoms to psychic influences); it should be remembered that hysteria and multiple sclerosis may co-exist; (2) from *Parkinson's disease* (age of patients; character of tremor and contracture; absence of nystagmus and of optic atrophy); (3) from *dementia paralytica* (age of patients; tremor not strictly intentional; speech disturbance is a syllable stumbling, not a scanning; characteristic psychic anomalies; lymphocytes increased and positive Wassermann reaction in cerebrospinal fluid); (4) from *tumor cerebri* (increased intracranial pressure; choked disk more common. Steady increase of symptoms, rather than remissions and exacerbations); (5) from *acute encephalitis* (course of disease); (6) from *Westphal's pseudosclerosis* (no optic atrophy; no true spasticity; early appearance of apathy and dementia; slowed movements of eyes and face); (7) from *diffuse cerebral sclerosis* (combination of progressive spastic paralysis with progressive dementia in childhood).

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## (*d*) *The Different Forms of Meningitis*

Inflammation may affect the dura mater (*pachymeningitis*), on its inner surface (*P. interna*), or its outer surface (*P. externa*), or it may affect the pia arachnoid (*leptomeningitis*).

### i. Pachymeningitis

#### (*1*) *Internal Hemorrhagic Pachymeningitis*

#### (*Pachymeningitis hemorrhagica interna, Hematoma durae matris*)

This is a vascular inflammation on the inner surface of the dura mater, which is rich in capillaries; thin, veil-like membranes are formed, which can be detached. The new capillaries are fragile and bleed easily. Recurring hemorrhages cause periodic exacerbations of symptoms; sometimes there is a lamination of the membrane, or a third (middle) membrane forms like a cap over the brain. The writer has seen one such case in a young child after typhoid fever.

The disease is most common in middle or advanced life, as a complication of chronic alcoholism or of dementia paralytica. Very large hemorrhages give rise to the so-called hematoma durae matris, the cushionlike clot occasionally seen at autopsy making round or oval depressions in the surface of the brain.

**Symptoms.**—There are none in mild cases. In severer cases, coma, preceded by excitement and unilateral convulsions with bradycardia and arrhythmia may occur; later, there is hemiparesis or monoparesis; choked disk and sometimes conjugate deviation of the eyes and head may be observable. Lumbar puncture may reveal blood in the cerebrospinal fluid. Remissions and exacerbations are common.

**Differential Diagnosis.**—From *cerebrospinal* or *tuberculous meningitis* (more rigidity of neck; involvement of cerebral nerves; cytodiagnosis after lumbar puncture).

### (2) *Chronic Hypertrophic Cervical Pachymeningitis*
### (*Pachymeningitis cervicalis hypertrophica*)

The dura in the region of the cervical enlargement of the spinal cord is thickened and compresses the nerve roots and the cord. The membrane may be six to ten times its normal thickness. It may become calcified or ossified. The process probably begins in the leptomeninges, rather than in the dura. Lues is the commonest cause.

**Symptoms.**—The disease begins with pains in the neck, and neuralgias in the domain of the N. ulnaris and N. medianus. After several months, paralysis with degenerative atrophy appears in the small muscles of the hand and in the flexors of the hand and fingers. As the extensor muscles, innervated by the N. radialis are not affected, there arises a characteristic attitude—dorsal flexion of the hand with flexion of the middle and terminal phalanges of the fingers (so-called "preacher's hand"). Anesthesia is usually slight. In late stages, spastic paraplegia of the legs develops (compression of the pyramidal tracts).

## ii. Leptomeningitis
## (*Pia-arachnoiditis*)

Several forms of inflammation of the pia-arachnoid are met with, including: (1) serous meningitis; (2) purulent meningitis; (3) epidemic cerebrospinal meningitis; and (4) chronic leptomeningitis (tuberculous and syphilitic meningitis are described under the specific inflammations of the nervous system).

### (1) *Serous Meningitis*
### (*Meningitis serosa, Primary Idiopathic Hydrocephalus of Oppenheim, Quincke's Disease*)

A meningeal inflammation with pure serous exudate is known as serous meningitis. The intracerebral pia alone may be involved (meningitis ventricularis), often giving rise to a *hydrocephalus internus* (acute or chronic); or the pia corticalis may be affected and give rise to a *hydrocephalus externus.*

The cause is unknown, though toxic and infectious influences, and trauma, have been suspected. The disease may develop acutely or slowly. Lumbar puncture shows a clear fluid, poor in cells, under high pressure. The clinical picture may be that of an acute acquired hydrocephalus (*q. v.*), or the disease may take an intermittent, chronic, course (headache, vomiting, optic neuritis, cerebellar ataxia, etc.). In some instances, it closely simulates brain tumor, giving rise to choked disk and optic atrophy, some-

times to hemi-anopsia bitemporalis (from dilatation of the floor of the third ventricle). But the remissions and intermissions lasting over years usually suffice to differentiate it, as well as the absence of focal symptoms (with the exception of ataxia). The cases of unilateral hydrocephalus, especially, simulate tumor.

**Differential Diagnosis.**—The acute form must be differentiated from other forms of meningitis (lumbar puncture); the chronic form from brain tumor (*vide infra*).

### (2) *Circumscribed Meningitis (Meningitis serosa circumscripta) in the Cerebellopontile Angle*

There may be pathological adhesions of the arachnoid to the cerebellum, in the region of the flocculus, leading to stasis in the cisterna lateralis pontis, which has its own plexus choroideus for the secretion of cerebrospinal fluid. As the pressure of the cerebrospinal fluid increases locally, it is likely that the pressure is propagated through the sheath of the N. acusticus into the labyrinth. The increased pressure in the cisterna lateralis can injure the N. acusticus, N. facialis, and N. trigeminus, sometimes, also, the N. abducens, N. glossopharyngeus, and N. vagus.

The symptoms that have been noted include, (1) tinnitus, (2) impairment of hearing, (3) vertigo, (4) depression of excitability on irrigation of external auditory canal (caloric nystagmus), (5) facial paresis, (6) suboccipital headache in and behind the mastoid process, due to injury to the nerves supplying the dura mater and the mucous membrane of the mastoid cells, (7) "pointing errors" on testing the wrist-joint, due to injury to the cortex of the cerebellum at the junction of the posterior with the inferior surface.

This has been described by Bárány as a special syndrome, more common in women than in men. The syndrome may arise in meningitis serosa, in otitic meningitis, in luetic, or in tuberculous, meningitis, and, occasionally, as a *"migraine otique"* (Escat), or as a "migraine of the posterior fossa of the skull."

Some of the simpler cases recover after lumbar puncture, though the explanation is not clear (rupture of the cistern?); a number of cases recover after exposure of the area by a decompression operation and opening of the cisterna (Placzek and Krause; H. Cushing; S. J. Crowe).

The condition should be differentiated (1) from *mastoiditis* (ear drum looks less normal; "pointing error" not present); (2) from *herpes of the N. acusticus,* so well described by J. Ramsay Hunt (herpes on the auricula; pointing error lacking); (3) from *sinus thrombosis* (tenderness behind the mastoid in sinus thrombosis is in the muscles, in the skin, or in the N. occipitalis major, and is not elicited solely when the pressure is made directly upon the bone as is the case in Bárány's syndrome); and (4) from *tumor of the cerebellopontile angle or of the cerebellum,* with which it is most often confused.

### (3) *Non-epidemic Purulent Meningitis*

### (*Meningitis purulenta*)

This often arises by extension (infections of the scalp, temporal bone, or along the vessels and nerves); sometimes it has a metastatic origin (pneumonia, bronchiectasis, putrid bronchitis, empyema, septic infections, acute rheumatism, influenza, etc.). When the inflammation extends to the spinal meninges, lumbar puncture will usually reveal the causal bacterium.

The symptoms are similar to those of epidemic meningitis (*vide infra*).

### (4) *Epidemic Cerebrospinal Meningitis*

### (*Meningitis cerebrospinalis epidemica, Cerebrospinal Fever, Meningococcal Meningitis*)

An infectious disease of the leptomeninges, due to the *Diplococcus intracellularis* (or *meningococcus*), commonly affecting young people, either sporadically, or in epidemics prevalent in the winter and in the spring.

**Symptoms.**—Onset usually sudden, with fever, violent headache and vomiting, photophobia, hyperesthesia acoustica, sometimes with a chill, or with a general convulsion. Rigidity and retraction of the neck appear early; Kernig's sign and Brudzynski's signs are positive (See Methods of Examination). The height of the temperature varies. The patient becomes delirious and the rigidity may extend to all the muscles of the body. Retention of urine or of fœces is common; sometimes there is incontinence. Eye-muscle paralyses may appear; sometimes, also, complicating infections of the eye. There may be paralysis of an extremity, or of half of the body. The deep reflexes are exaggerated at first; they often disappear later. Skin eruptions (erythema, roseola, purpura and especially herpes) are common during the first few days ("spotted fever"). In fatal cases, the coma deepens and respiratory and circulatory disturbances appear. Mild cases, and especially those treated with Flexner's serum, may recover without residue. With Flexner's serum, 75 per cent recover and 25 per cent die; without it, the figures are reversed. Severe cases that recover show residues (paralyses, deafness, aphasia, blindness, etc.).

**Complications.**—Arthritis, pleuritis, bronchopneumonia, endocarditis, panophthalmitis.

**Course.**—The fulminating type (*forme foudroyante*) may kill in a few hours. Abortive forms, with slight headache or pain in the neck or back, and possibly vomiting, lasting a few days, occur during epidemics; outside of an epidemic they would go unrecognized unless a lumbar puncture were made. Cases running a prolonged course (many

weeks), with intermittence of the fever and of the other symptoms, are not uncommon.

**Differential Diagnosis.**—(1) From *other forms of meningitis* (absence of herpes, co-existence of other infections, lumbar puncture shows pneumococci, streptococci or influenza bacilli); (2) from *meningismus* in typhoid, pneumonia or sepsis (absence of herpes, criteria of primary disease, lumbar puncture); (3) from *acute articular rheumatism;* (4) from *tetanus.*

The disease is described more fully among the Infectious Diseases (See Part IV).

### (5) *Chronic Leptomeningitis*

This disease occurs in chronic alcoholism, and in dementing processes, as a simple inflammation. Chronic basal meningitis is usually syphilitic in origin, though a simple primary type is described (persistent headaches, with paroxysmal exacerbations, vomiting and occasional convulsive seizures, vertigo, slight fever and optic neuritis, leading to atrophy and various cerebral nerve paralyses). Many of these cases were doubtless instances of the meningitis serosa circumscripta above described.

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## 2. Diseases Due to Specific Inflammations (Infectious Granulomata) of the Central Nervous System and Its Meninges

These include the (a) tuberculous, (b) luetic, (c) actinomycotic and (d) leprous inflammations.

### (a) *Tuberculosis of the Nervous System*

The most important forms clinically are: (1) tuberculous meningitis; (2) conglomerate tubercle of the brain; (3) tuberculous pachy- and peripachymeningitis.

#### i. Tuberculous Basilar Meningitis

*Meningitis tuberculosa*

**Definition.**—A tuberculous infection of the leptomeninges, secondary to primary tuberculosis elsewhere (lungs, pleura, lymph glands, bones, genito-urinary tract); common in childhood (second to fifteenth year); extremely rare after forty. Measles and whooping-cough are predisposing infections.

The tubercles are most numerous at the base of the brain (basilar meningitis), and the exudate (serous, fibrinous or purulent) also accumulates at the base. When miliary tubercles predominate, we speak of miliary tuberculosis of the meninges; when the exudate is prominent, we speak of tuberculous meningitis.

**Symptoms.**—Onset insidious, in pale feeble children, the prodromata (emaciation, anorexia, constipation, disturbed sleep) lasting for weeks. Then come headache, apathy, fever, projectile vomiting; and, later, delirium, drowsiness, slowed, irregular pulse, gritting of the teeth, rigidity of the neck, and general hyperesthesia. Still later, the abdomen is retracted (boat-shaped). The pupils become unequal and sluggish to light. There may be choked disk, and, occasionally, tubercles are visible in the choroid. Gradually sopor intervenes, with tachycardia; the pupils dilate, and cerebral nerve involvement becomes obvious (ptosis, facial paresis). Finally, coma sets in, with Cheyne-Stokes breathing; transitory monoplegia, hemiplegia, or aphasia, and often convulsions appear before death. For the findings in the cerebrospinal fluid, see Exploratory Punctures.

The duration varies; death in most cases occurs within three weeks after the symptoms of meningeal irritation appear. A few cases terminate fatally within a few days; now and then a patient drags on for months with remissions. A few cases proved undoubtedly tuberculous by demonstration of the presence of tubercle bacilli in the fluid on lumbar puncture have recovered.

The atypical cases, especially in adults, are often wrongly diagnosed.

**Differential Diagnosis.**—In children with bad heredity, or scrofula, or in the convalescence from measles or whooping-cough, the appearance of apathy, unmotived vomiting and slow, irregular pulse should make one think always of basilar meningitis. The disease is sometimes confused with: (1) *gastro-intestinal catarrh* (lumbar puncture negative); (2) *meningismus* of typhoid fever (bacillus typhosus in blood culture; positive diazo and Widal, negative lumbar puncture, no choroid tubercles);

(3) *uremia* (urinary findings, retinitis, lumbar puncture); (4) *general miliary tuberculosis* (prominent pulmonary phenomena, tachypnea and tachycardia from the beginning; (5) *other forms of meningitis* (shorter prodromal stage, cocci on lumbar puncture, absence of choroid tubercles).

### ii. Conglomerate Tubercles of the Brain

*(Solitary Tubercle)*

In children, one half of the intracranial new growths, so-called brain tumors, are not true tumors but tuberculous growths; in adults, about one-seventh. Solitary tubercle is commonest in the cerebellum, but it is also common at the base of the brain, and in the brain stem. It is often the cause of hydrocephalus, through pressure on the vena magna Galeni or on the aqueductus cerebri. The foci are multiple in 25 per cent of the cases. Large masses may be present without causing symptoms; in other cases, a small mass may cause cortical epilepsy or a monoplegia.

### iii. Tuberculosis of the Dura Mater and of the Extradural Tissues

*Pachy- and Peripachymeningitis tuberculosa*

This is common in caries of the spine, and often gives rise to compression of the spinal cord (*q. v.*).

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### (*b*) *Syphilis of the Nervous System*

(*Cerebrospinal Syphilis, Lues cerebrospinalis*)

Clinically, the most important forms are: (1) gummatous meningitis; (2) gummatous arteritis; (3) luetic meningo-encephalitis and meningo-myelitis. They may all be summed up in the term cerebrospinal syphilis (*lues cerebrospinalis*). From the foregoing, we distinguish the para-syphilitic diseases (tabes, dementia paralytica), though these are also due to infection with the *Treponema pallidum.*

Basal gummatous meningitis is the form most often encountered. It varies in extent, and is often accompanied by arterial changes and by involvement of the cerebral nerves at the base.

**Symptoms.**—Headache, with nocturnal exacerbations, vomiting, vertigo, sometimes attacks of unconsciousness and general convulsions; psychic symptoms (loss of memory, mental deterioration, apathy). Most striking is the great *oscillation of the symptoms,* especially an alternation of delirium with coma. Cerebral nerve paralyses (especially Nn. III, IV and VI) are common. 1. Unilateral or bilateral optic neuritis or choked disk, optic tract lesions, anosmia, facial palsy, deafness, polydipsia and polyuria, focal symptoms due to arterial lesions (hemiplegia, aphasia, hemi-anopsia, etc.) are among the phenomena that may appear. The recurring remissions and exacerbations are very characteristic.

Occasionally, the luetic process attacks the meninges of the convexity (focal symptoms), or the spinal meninges and the spinal cord itself may be more affected than the brain. Luetic thrombo-arteritis may cause myelomalacia with incomplete transverse lesion of the cord.

Cerebrospinal syphilis is a common disease, and because of the possibility of influencing its course by therapeutic measures its diagnosis is of unusual importance.

The pathological basis of the disease consists of the syphilitic infiltrations and gumma formations that affect the vascular system, the meninges, and the white and gray matter of the brain and cord. Non-specific secondary changes (hemorrhage, softening, pressure atrophy) likewise occur and are no less important in the production of symptoms.

Because of the lawlessness of the occurrence of syphilitic lesions in the central nervous system, all clinical classifications of these cases are based only on the predominance of certain associations of lesions. The cases in which the lesions are chiefly *cerebral* may be subdivided into types that are chiefly vascular, chiefly meningeal, or chiefly due to intracerebral gummata. The *spinal* cases fall into (1) those in which the symptoms are chiefly due to meningeal involvement and (2) those in which the consequences of myelitis are in the foreground.

**The Vascular Type of Brain Syphilis.**—The essential feature in the pathology

of syphilitic arteritis in the brain is a proliferation of the intima, which, by gradually narrowing the lumen of the vessel, tends to cause thrombosis with consequent formation of areas of anemic infarction. This sequence of events is most common in the domain of the A. cerebri media, with the production of hemiplegia, and of aphasia. It not infrequently affects the A. basilaris (pontile or bulbar foci, with corresponding symptoms; sometimes hemiplegia cruciata), the A. cerebri posterior or its branches (hemi-anesthesia, hemi-anopsia), the A. vertebralis (unilateral bulbar paralysis with hemi-anesthesia of the same side and hemiplegia of the opposite side).

Clinically, these paralyses are characterized by a tendency to occur gradually and with very few symptoms of cerebral insult. Not infrequently, they occur stepwise during the course of several days. In the distribution of the paralysis, or in the type of the aphasic disturbances, there is, however, nothing characteristic. Recovery is perhaps more often complete than in non-syphilitic cases, but there is a marked tendency to recurrence.

**The Meningeal Type of Brain Syphilis.**—Syphilitic meningo-encephalitis. The leptomeninges of the base of the brain, or of the convexity, or of both, may be involved in a syphilitic, infiltrative process with gumma formation. The small nutrient vessels of the cortical gray matter and the perivascular lymph spaces show degeneration of their endothelial cells and round-celled infiltration, so that the process is best termed a *gummatous meningo-encephalitis.*

Headache, often worse at nights, is a common feature in these cases. In some instances other symptoms of increased intracranial pressure are observed (choked disk, slow pulse, nausea and vomiting, dizziness, sopor, delirious states). But in the less acute cases, all these manifestations are frequently absent. The base of the brain, especially in the region of the middle fossa of the skull, is most frequently affected in *luetic meningitis.* Multiple lesions of the cerebral nerves result either from pressure effects of the exudate, or of gummata, or by direct invasion of the nerves themselves or of their roots by the syphilitic process. Optic neuritis, choked disk, optic-tract lesions, anosmia, paralyses of the ocular muscles, facial neuralgias, facial palsy, deafness, anarthria etc., are characteristic effects. There is a marked tendency to variability and to remissions of the symptoms, especially under the influence of specific therapy.

The involvement of the cortex in *meningo-encephalitis of the convexity* leads, in some cases, to mental deterioration. When the motor areas are affected, a monoplegia may be produced. Epileptic attacks, of the jacksonian type, are not infrequently observed; they differ in no wise from those due to tumor or to any other irritative lesion. A residual palsy may point to the site of the lesion.

**Isolated Gumma of the Brain.**—Large single gumma in the white or gray matter of the brain produces no symptoms distinguishable from those of any other new growth in the same position. The results of therapy are seldom marked enough to be of diagnostic value. The condition is comparatively rare.

**Syphilitic Meningomyelitis.**—Syphilis of the cord and its meninges is usually accompanied, sooner or later, by evidences of a meningo-encephalitis. The vessels of the cord are affected similarly to those of the brain, but there is almost always an accompanying meningitis and myelitis of gummatous type.

The symptoms in these cases are due in part to involvement of the roots of the spinal nerves, in part to involvement of the cord itself that gives rise to the picture of partial or complete transverse lesions. There are also rarer cases in which degenerations of the long conduction paths yield syndromes analogous to the non-specific system diseases.

The roots of the spinal nerves may be compressed by the exudative thickening of the leptomeninges, or a syphilitic endoneuritis may occur. Paresthesias, hyper-

esthesias, or severe persistent neuralgic pains may result in the distribution of the nerve roots so affected (intercostal neuralgia, sciatica, etc.). Atrophy of the corresponding muscles follows. In the upper region of the cord, a localized proliferative syphilitic meningitis gives rise to the condition known as *pachymeningitis cervicalis hypertrophica* (*q. v.*)

Foci of softening in the substance of the cord may arise from syphilitic thromboarteritis, the cord may be compressed by meningeal proliferative changes, or gummata may occur in the white or gray matter. Symptoms of complete or incomplete transverse lesions result with atrophic paralyses at the level of the lesion and spastic paralyses below. Paraplegia of the lower extremities, sphincter disturbances, and partial Brown-Séquard syndromes are common. In some instances, the onset is very acute resembling that seen in non-luetic myelitis.

Attempts have been made to erect system disease syndromes analogous to tabes; but occurrences of primary degenerations of the long conducting tracts due to supposed syphilitic toxins is certainly rare. The best established type is *Erb's syphilitic spinal paralyses* (*q. v.*) characterized clinically by spastic paralyses of the lower extremities, spastic gait, and increased tendon reflexes, with no involvement of the upper extremities, or of the cerebral nerves or the psychic functions. In some cases, this condition is apparently due to a true system disease on a syphilitic basis, analogous to tabes; there are non-specific degenerative changes in the pyramidal tracts, the lateral cerebellospinal tracts and in Goll's column. The same syndrome may occur, however, during the development of a diffuse syphilitic meningomyelitis. In some cases of progressive muscular atrophy, a syphilitic basis for the degenerative changes in the anterior-horn cells has been apparent.

**Diagnosis of Cerebrospinal Syphilis.**—The diagnosis of cerebrospinal syphilis is usually not difficult. The examination of the spinal fluid and blood, the presence of pathognomonic signs, or of suggestive clinical syndromes, or of lesions of syphilis elsewhere in the body, and the results of anti-luetic therapy are all of great value in arriving at a decision.

The most decisive data are obtainable from the examination of the spinal fluid. A positive Wassermann reaction in the spinal fluid is conclusive evidence of involvement of the central nervous system by a syphilitic process. A well-marked syphilitic type of precipitation of the gold-sol appears to have a similar value. Lymphocytosis and positive Phase I are chiefly of value as confirmatory evidence of syphilis. The blood Wassermann can of course be considered only as supporting evidence and in no way as direct proof of the involvement of the nervous system. In cerebrospinal syphilis, the Wassermann reaction is positive in the blood in 70-80 per cent of the cases. In the spinal fluid using 0.2 c.c. it is positive in only about 20 per cent of the cases, but by the use of larger amounts (0.8-1.0 c.c.) it is positive in 95-100 per cent of the cases.

Recent studies of the spinal fluid in syphilis have made it evident that syphilis of the nervous system is often present for a time without symptoms, as a form of latent syphilis. The diagnosis of this condition is of the utmost importance and can be made only by examination of the spinal fluid. No case with a history of syphilitic infection, or other evi-

dence of such infection, can safely be pronounced free from this disease, unless an examination of the spinal fluid with negative results has been made as one of the criteria of cure.

The Argyll-Robertson pupil (reaction to accommodation but not to light) is pathognomonic of syphilis of the nervous system. It is, however, more commonly found in tabes and in paresis than in the cases of ordinary cerebrospinal syphilis.

Certain clinical syndromes should always suggest syphilis of the nervous system. Hemiplegia occurring in patients under forty in whom no cardiac or renal lesions are present is almost always due to cerebral syphilitic arteritis with secondary thrombosis. In young people, the gradual development of a spastic paraplegia of the lower extremities without sensory changes will frequently be found due to syphilis of the cord. Of all eye-muscle palsies, over one-half are due to syphilitic meningo-encephalitis.

Very characteristic of syphilitic lesions is their tendency to periods of regression, to recurrences and to changes in distribution. Similar fluctuations in symptoms, temporary palsies, shifting root pains, marked remissions in symptoms of intracranial pressure, should always suggest cerebrospinal syphilis.

In attempting to establish a syphilitic etiology signs of syphilis elsewhere in the body are of course of value. It is astonishing, however, how frequently they may be entirely lacking. Perhaps the commonest association is that between syphilitic aortitis (Heller-Döhle), with aortic insufficiency or aneurism, and cerebral vascular syphilis, either manifest or latent.

The diagnosis of cerebrospinal syphilis *ex juvantibus* is usually very unsatisfactory. The secondary results of vascular and even gummatous lesions are often quite irreparable. It is only in the rarer cases, where the resorption of gummatous lesions leads to striking and permanent improvement, that much stress can be laid on the therapeutic test.

**Differential Diagnosis.**—The condition must be differentiated from (1) *cerebral tumor;* (2) simple *cerebral atherosclerosis;* (3) *multiple sclerosis;* (4) the functional nervous disorders (*neurasthenia, hysteria*); (5) in the spinal form, from *simple myelitis,* and from *compression-myelitis.*

In all cases, the signs of multiple lesions, and the marked oscillation of the symptoms, favor the diagnosis of cerebrospinal lues.

### (c) Actinomycosis and Leprosy of the Nervous System

These are extremely rare diseases. The diagnosis depends also upon signs of these infections elsewhere in the body.

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# F. Diseases of the Nervous System Due to Disturbances of the Lumen

The lumen of the central nervous system consists of the central canal of the spinal cord, the fourth ventricle, the aqueductus cerebri, the third ventricle and the lateral ventricles. Dilatation of the ventricles of the brain is known as *internal hydrocephalus;* simple dilatation of the central canal of the cord as *hydromyelia.*

## 1. Hydrocephalus

The dilated ventricles may be filled with clear fluid (*simple hydrocephalus*), or with a turbid exudate (*inflammatory hydrocephalus*). Pressure-atrophy of the brain results, and the upper part of the skull becomes distended, making the facial skull look relatively small and triangular. Most cases are congenital; others are acquired.

### (*a*) *Congenital Hydrocephalus*

(*Hydrocephalus congenitus*)

This is often combined with agenesia of the brain, hairlip, clubfoot, or spina bifida. When intra-uterine, it may be an indication for craniotomy.

The amount of fluid may vary from a few hundred cubic centimeters to ten or twelve liters, averaging, perhaps, one liter.

**Symptoms.**—Besides the alteration in the size and shape of the skull, the disease is accompanied by defective cerebral function (arrested development, idiocy or imbecility, late and clumsy walking, spastic paraparesis, choked disk, neuritic optic atrophy, premature puberty). Röntgenograms of the skull are characteristic.

**Differential Diagnosis.**—From *rickets*, affecting the skull (quadrangular, box-shaped skull; other signs of rickets; absence of cerebral symptoms; x-ray findings).

Fig. 616.—Chronic Hydrocephalus in a Ten Months' Child. (After M. Rothmann, "Handb. d. inner. Med.," published by J. Springer, Berlin.)

Fig. 617.—Hydrocephalus and Spina-bifida. (Med. Service, J. H. H.)

### (*b*) *Acquired Hydrocephalus*

(*Hydrocephalus acquisitus*)

This may arise at various ages, acutely or slowly, (1) from basal meningitis with involvement of the choroid plexus, (2) from inflammatory closure of the foramen of Magendie or of the aqueductus cerebri, (3) from simple stasis due to closure of the lumen, (4) from pressure of

tumors, or (5) from sinus thrombosis. The cases secondary to tumor and other compressing influences are separable from the so-called primary iodiopathic hydrocephalus described as meningitis serosa (*q. v.*).

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## 2. Hydromyelia

This condition is rare and practically has but little clinical significance.

The form of cavity formation known as syringomyelia (*q. v.*) is due to the breaking down of a tumor (glioma), not to a primary disturbance of the lumen.

# G. Diseases of the Nervous System Due to Interruptions of Continuity

## 1. Trauma of Brain Due to Fracture of Skull, Gunshot Wounds, etc.

The diagnosis is usually easy from the history of the case, the signs referable to the nose and ears, palpation and x-ray examination of the skull.

Focal symptoms may point to injuries of specific regions of the brain.

## 2. Traumatism and Compression of the Spinal Cord

*Fracture of the spine* is commonest in the lumbar region, *dislocation* in the cervical region. *Stab wounds* and *shot wounds* occur at various levels and often cause Brown-Séquard paralysis (*q. v.*).

Traumatic injuries to the spinal cord may cause complete transverse lesion, or incomplete transverse lesion, the symptoms depending upon the level (See Topical Diagnosis). Röntgenograms reveal the bone lesions.

In the absence of actual fracture or dislocation there may be serious injury from *commotio spinalis* (Erichsen's disease), giving rise to the symptoms usually designated as those of a *traumatic neurosis.*

### (*a*) *Hematomyelia*

As a result of trauma, hemorrhage into the cord (hematomyelia) may occur, especially in the cervical region. The blood is most often shed into the gray substance; it tends to spread in the longitudinal direction (tubular hemorrhage, or pencil-shaped hemorrhage). The symptoms resemble those of syringomyelia (*q. v.*). The history of the case, however, will permit of differentiation.

### (*b*) *Compression of the Spinal Cord and Nerve Roots Due to Vertebral Diseases*

The spinal canal may be encroached upon by tumors, exostoses, inflammatory exudates, hemorrhages or echinococcus-cysts, but the most common cause of compression myelitis is tuberculous caries of the spine with peripachymeningitic granulation tissue, or the development of an angular kyphosis (gibbus), from telescoping of the vertebrae; either may lead to slow compression of the spinal cord.

#### i. Compression of the Spinal Cord and Nerve Roots from Pott's Disease of the Spine

(*Spondylitis tuberculosa*)

This is common in childhood and in adolescence, but may occur at any age. I have seen it more than once in elderly people. The compression may be due to a tuberculous abscess without change in the form of the spine; generally a projecting knuckle (gibbus), or angular kyphosis, is demonstrable, owing to telescoping of the softened carious parts of the vertebrae.

**Symptoms.**—These depend upon the site of the lesion (See Topical Diagnosis of Lesions of the Spinal Cord).

The thoracic part of the cord is most often involved, the malady beginning with pain in the back, or intercostal neuralgia, sometimes with

spastic paresis of the legs and exaggeration of the knee-kicks. Motor disturbances predominate; sensory symptoms may be slight or absent. The sphincter functions are early disturbed. Psoas abscess or cold abscesses in other positions may develop (See part XI).

In cervical caries, the signs of myelitis cervicalis may develop with "root pains" in the neck, or in the upper extremities. In caries of the uppermost cervical spine and of the atlanto-occipital joint (*malum suboccipitale*), the first symptom is pain in the head and neck with rigidity, and sometimes crepitation. Unilateral, or bilateral, occipital neuralgia may be complained of. There are symptoms, sometimes, referable to N.XI or N.XII. Occasionally a retropharyngeal abscess (visible and palpable) develops.

**Differential Diagnosis.**—The condition most likely to be mistaken for Pott's disease is *metastatic carcinoma of the spine* (search for primary carcinoma of breast, rectum, prostate, etc., especially in advanced life; absence of tuberculosis of other organs, of psoas abscess, etc.). Occasionally, meningeal *tumors*, *lues spinalis,* or *aortic aneurism*, destroying the spine, may give similar symptoms. I have recently seen a young school teacher, treated for a year for "rheumatism," who, on examination, showed a large thoraco-lumbar gibbus and signs of a left-sided tuberculous pleurisy!

### ii. Compression of the Spinal Cord or Nerve Roots Due to Cancer and Other Tumor Involving the Spine

Carcinoma of the spine is always metastatic, the primary tumor being situated in some epithelial organ (breast, uterus, prostate, thyroid, stomach, pancreas, etc.). When root symptoms exist, inquiry should be made regarding a preceding breast operation. Sarcoma, or osteosarcoma, of the spine may be primary.

Severe neuralgic pains in the spine, especially bilateral intercostal neuralgia, and bilateral sciatica, with or without herpes, should excite suspicion. The root pains usually precede the paralytic symptoms; the former are due to irritation of the posterior roots, the latter to compression of the cord. Many of these cases are at first mistakenly thought to be *neurasthenic* or *hysterical;* others are wrongly diagnosed as *caries,* still others as *spinal lues.*

### iii. Compression of Nerve Roots in Arthropathies of the Spine

The vertebral joints may be the site of an acute or subacute infectious arthritis (gonorrheal, rheumatic, luetic, tuberculous), or of a chronic arthritis of which there are two main varieties (1) ankylosing arthritis of the spine (*spondylitis ankylopoietica*), and (2) hypertrophic osteo-arthritis (*spondylitis deformans*). (See Part XI.)

These processes may involve one or several joints of the spine. In the worst form, bony deposits extend along the spine, ankylosing it (poker spine). The conditions are more fully described under Diseases of the Bones and Joints, but are mentioned here on account of the accompanying neural involvement.

**Symptoms.**—Radiating root pains are common, giving rise to intercostal, brachial, crural or sciatic neuralgias (posterior roots). There may be partial segmental atrophic paralyses (anterior roots). In the neuralgic area there may be herpes.

The diagnosis is usually easy, owing to limitation of the movements of the spine, the simultaneous presence of arthritis in the joints of the extremities (not always), the characteristic root symptoms, and the x-ray examination.

The so-called typhoid spine is usually due to infectious arthritis (T. McCrae). An attempt has been made to establish definite types of the ankylosing form: (1) the *Strümpell-Marie type,* in which the joints of the spine are involved along with the hip-joints or shoulder-joints, without involvement of the smaller joints of the extremities; and (2) the *Bechterew type,* in which there is anchylosis of the spine with thoracic kyphosis and root pains, without involvement of the hips and shoulders. No sharp distinction is, however, justifiable (See also, Part XI).

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## H. Diseases of the Nervous System Due to Invasion by Animal Parasites

The animal parasites to be considered here include: (1) *Cysticercus,* (2) *Echinococcus,* (3) *Trypanosoma,* (4) *Plasmodium malariae.*

### 1. Cerebrospinal and Ocular Cysticercus

This condition has become less common since pork inspection has been more general and invasion of the intestine by *Taenia solium* occurs more rarely.

The brain may be studded with hundreds of the vesicles. Occasionally, the cerebrospinal meninges may be invaded (*cysticercus meningitis*). The cysticerci may live from three to twenty years in the brain. Floating cysticerci in the third or fourth ventricle occur. Cysticerci may also invade the vertebral canal and cause a compression of the cord.

**Symptoms.**—Often indefinite (paroxysmal headache, vertigo, disturbance of consciousness). A cysticercus epilepsy is known. Cerebral spasms general or local, depending upon the localization of vesicles are common. A cysticercus in the fourth ventricle may give rise to a combination of symptoms referable to the cerebellum and the medulla oblongata (vertigo, vomiting, cerebellar ataxia, glycosuria, disturbances of the heart and of the respiration); alternation of periods when these symptoms are present or absent (Bruns' symptom) suggests a floating cysticercus of the fourth ventricle.

**Differential Diagnosis.**—A probable diagnosis may be made if the symptoms have been preceded by (1) opportunity for infection (eating raw pork, occupation); (2) a history of tapeworm; (3) the discovery of cysticercus nodules in the skin or in the muscles (histological examination), or of cysticercus oculi. The patients are nearly all males, over forty years of age.

The condition is likely to be confused with (1) brain tumor; (2) lues cerebrospinalis; or (3) psychoneurotic states.

## 2. Echinococcus Disease of the Nervous System

A very rare disease, more often unilocular than multilocular. It gives rise to symptoms similar to those of tumor cerebri, and the true cause is usually recognized first on operation, or at autopsy. Occasionally, it may be suspected during life from (1) the presence of echinococcus cysts in other organs; (2) exposure to invasion through companionship with dogs; or (3) the finding of hooklets in the cerebrospinal fluid on lumbar puncture.

## 3. Trypanosomiasis of the Nervous System

(*Sleeping Sickness*)

The infection occurs through the bite of a fly (*Glossina palpalis*), the fly having become infected from man or from diseased crocodiles.

In the first stage of the disease, the small, fishlike flagellates (*Trypanosoma gambiense*) are actively motile in the blood, causing an irregular fever (trypanosome fever). After some months the trypanosomes invade the nervous system and subarachnoid space and give rise to sleeping

sickness. Finally, death results from coccal infection of the meninges and purulent meningitis (See Diagnosis of the Infectious and Parasitic Diseases).

**Diagnosis.**—The trypanosomes are present in the cerebrospinal fluid obtained by lumbar puncture, and also in the juice of the cervical lymph glands in 80 per cent of the cases.

### iv. Cerebral Malaria

See Malaria (Part IV).

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[See also References on Sleeping Sickness and Malaria in Part IV.]

# I. Diseases of the Nervous System Due to Tumors

## 1. Varieties of Tumors

A few tumors are primary in the nervous system (glioma, ganglioneuroma). Others are primary in the nerve roots (neurofibroma), in the meninges (sarcoma, endothelioma, angioma), or in the bones of the skull and spine (osteosarcoma, chondroma, etc.), and injure the nervous system by pressure or invasion by extension. Still others are metastatic or secondary tumors in the nervous system or its covering from primary tumors (carcinoma, sarcoma) of other organs. A few tumors are certainly embryonic inclusions (teratomata, dermoid cysts, cholesteatomata).

**Glioma** is primary in the neuroglia of the nervous system (including the retina). It has nothing to do with sarcoma. It is the commonest tumor of the brain, varying in size from that of a pin's head to that of an apple. It is not sharply circumscribed, as it infiltrates the surrounding tissues diffusely. It is very subject to hemorrhage, degeneration and cyst formation, grows slowly (for years or decades), rarely gives rise to metastases, and causes symptoms by dislocation of healthy parts and increased intracranial pressure. In the spinal cord, it arises in the gray matter, spreads along the long axis as a pencillike column, and, through

degeneration, gives rise to cysts (*syringomyelia*). A hyperplasia of the neuroglia in the cord (in contrast with true glioma spinalis or gliomatosis) is known as *gliosis spinalis.*

**Ganglioneuroma,** or **true neuroma,** is a tumor containing newly formed ganglion cells. Such tumors are found in the domain of the sympathetic nervous system and the adjacent chromaffin system. The majority of them have been met with in children in the region of the adrenal. They vary in size from that of a cherry to that of a child's head.

**Neurofibroma** (false neuroma) is really a fibroma arising in the connective tissue of nerves. Single nerves, or nerve roots, may be involved, or several branches of a nerve may be thickened (*neuroma racemosum plexiforme; elephantiasis congenita*), or, most important clinically, great numbers may appear diffusely on the roots of the cerebral or spinal nerves, and in the peripheral nerves all over the body (*multiple neurofibromatosis, neurofibromatosis generalis, von Recklinghausen's disease*). When the cutaneous nerves are implicated the condition is called *fibroma molluscum multiplex.*

It is this tumor that affects the nervus acusticus at the cerebellopontile angle; the N. trigeminus is also frequently involved.

Primary **sarcoma** arises either in the meninges or in the sheaths of the blood vessels of the brain and cord; **osteosarcoma** from the bones of the skull or from the vertebrae. A remarkable form is the **diffuse sarcomatosis of the meninges** spreading over the nerve roots of the spinal cord or the base of the brain.

**Endothelioma** arises from the endothelium of the blood and lymph vessels or from the endothelium lining the meninges and pacchionian granulations. The tumors may reach a large size (goose egg, apple), and are often multiple, invading the brain or the skull and scalp. Small endotheliomata may undergo hyaline transformation and calcification, giving rise to the so-called sand tumors **(psammomata).**

Secondary carcinoma or sarcoma of the central nervous system and meninges is not rare. Clinically, **secondary carcinoma of the spine,** with involvement of the nerve roots, is the more important.

Inflammatory masses (solitary tubercle, gumma or syphiloma) in the nervous system or its meninges often give rise to symptoms scarcely distinguishable from those caused by tumors.

## 2. Rapidity of Growth, Multiplicity and Anatomical Effects of Tumors

**Rapidity of Growth.**—Some tumors grow very slowly, especially gliomata (years or decades), osteomata and angiomata; some, like soft sarcomata and carcinomata, grow rapidly. Steady progression (fast or slow) is characteristic of tumor growth, in contrast with the remissions and exacerbations of luetic growths.

**Multiplicity of Tumors.**—Gliomata are usually single; sarcomata also, but not always; epitheliomata may be single or multiple. Inflammatory non-neoplastic new growths, like tubercle and gumma, are often multiple.

**Anatomical Effects of Tumors.**—Tumors may infiltrate, compress, or dislocate nerve structures, either directly, or within the skull, by general increase of intracranial pressure. By compressing veins, closing foramina or the aqueduct, they may cause *hydrocephalus* and hypertension of the cerebrospinal fluid, the latter leading to increased pressure in the pial sheath of the nerves—in the optic nerve causing *choked disk* and *optic atrophy;* in the acoustic nerve causing *choked labyrinth* and *deafness;* in the posterior roots of the spinal nerves causing *choked*

*spinal roots,* and degeneration of the posterior funiculi. The bones of the skull may become thin (*pseudoporosis*).

**Symptoms.**—It will be convenient to consider intracranial tumors apart from intraspinal tumors. Clinically, too, it is necessary to consider together (1) the tumors of the nervous system proper (tumor cerebri, tumor cerebelli, tumor medullae spinalis), (2) tumors of the meninges, and (3) tumors arising in the bones and extending to the meninges and nervous system. Along with these, some mention must also be made of (4) inflammatory growths (gumma, tubercle), which, though not tumors, give rise to similar symptoms.

## 3. Symptoms of Intracranial Growths

Gliomata and other intracranial growths (neoplastic, inflammatory, aneurismal) may give rise both to general and focal symptoms.

### (a) *General Symptoms Suggestive of Intracranial Growths*

The general symptoms of intracranial growth include:

1. Choked disk (90 per cent of cases).
2. Headache.
3. Vomiting.
4. Mental dullness.
5. Vertigo.
6. Bradycardia.
7. General convulsions.

**Choked Disk.**—Since choked disk is so common in brain tumors the ophthalmoscopic examination should never be omitted in suspected cases. Some authors do not distinguish between optic neuritis and choked disk. Clinically it is convenient to reserve the term choked disk for cases in which there is marked swelling (2 diopters or more) and enlargement of the papilla. The presence of true choked disk (in the sense mentioned) makes the diagnosis of tumor cerebri very probable, though true choked disk may also occur in different forms of meningitis, in brain abscess, in lues cerebri, and in hydrocephalus. It is sometimes found also in chlorosis, in nephritis, and in chronic lead poisoning.

An optic neuritis, with a swelling of the disk of less than two diopters, may arouse suspicion, but it has nothing like the diagnostic value of true choked disk. Optic neuritis occurs frequently in infectious diseases, in toxic disturbances of various kinds, and in orbital diseases, in all of which it is often unilateral rather than bilateral. It may be present in renal

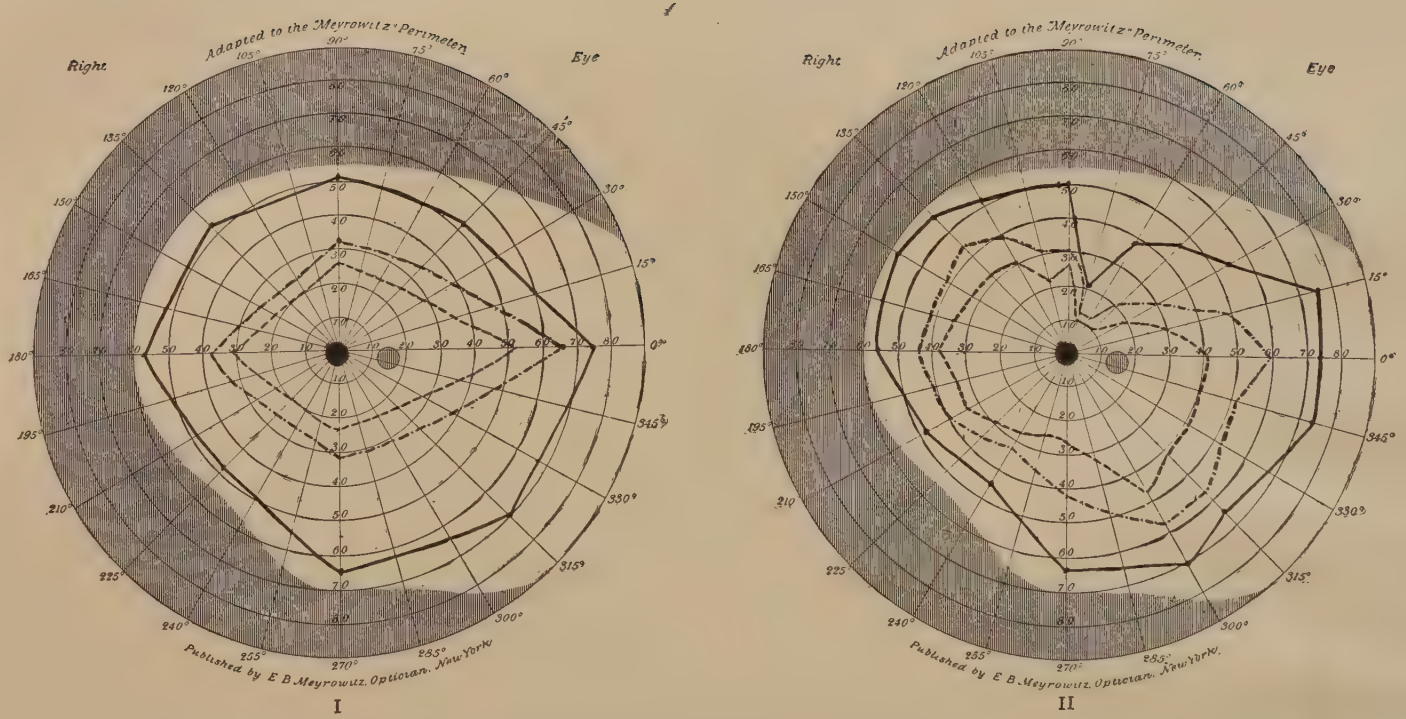


Fig. 618.—Illustrating the Importance of Careful Perimetric Charts in Cases of Brain Tumor. I, Using Few Points in the Visual Field, Considered Normal; II, Disclosing Upper Right Temporal Defect. (After H. Cushing and G. H. Heuer, J. H. H. Bull.)

disease, but then the surrounding retina is also altered (albuminuric retinitis). One meets with it, further, in multiple neuritis, in acute encephalomyelitis, and occasionally, though rarely, in multiple sclerosis. The so-called retrobulbar neuritis (developing acutely in multiple sclerosis, or more slowly in various intoxication amblyopias due to alcohol, tobacco, carbon bisulphid, etc., and in diabetes) does not yield the ophthalmoscopic picture of neuritis optica; the papilla is for a long time scarcely changed at all, though finally retrograde atrophy occurs, usually on the temporal side, causing the so-called temporal pallor of the disk.

The choked disk may be absent at the beginning of cerebral tumors of any kind and may continue absent during the course of small growths, cystic growths, diffuse extracerebral growths, or in tumors of the motor area, of the pons, or of the medulla oblongata.

**Headache.**—This, if long continued and violent, should arouse suspicion. One looks for other causes, such as (1) cerebral atherosclerosis; (2) diseases of the heart or of the digestive organs, especially chronic constipation; (3) intoxications (tobacco, arsenic, lead, copper, mercury, etc.); (4) the morphin habit or other drug habit; (5) Graves's disease; (6) psychoneurotic states (migraine, hysteria, neurasthenia).

**Vomiting.**—This is helpful for diagnosis only when it is "cerebral" in character (projectile, unmotived).

**Mental Dullness.**—The drowsiness and dulling of consciousness are important signs, but of course may be due not to brain tumor but to (1) a psychosis, or (2) some intoxication (uremia, cholemia, diabetic coma).

**Vertigo.**—Very little stress should be laid upon this symptom unless it is accompanied by other general symptoms (see Vestibular Syndromes).

**Bradycardia.**—Slowing of the pulse may be an important sign of increased intracranial pressure, but the increase of pressure may not be due to a brain tumor. Bradycardia occurs also in atherosclerosis, in heart block, in vagal hypertony from various causes, and sometimes, in hypothyroidism.

**General Convulsions.**—These may be of the type of true epilepsy; indeed, many patients regarded as simple epileptics for years (10–30) may be the victims of a slowly developing brain tumor (osteoma, glioma, solitary tubercle). Convulsive seizures, resembling hysterical attacks or tetanic rigidity, may also occur, the latter especially in tumors of the posterior fossa of the skull.

**Röntgenography of Skull.**—Heuer and Dandy (1916) have made a special study of the x-ray findings of the skull in 100 cases of brain tumor and other intracranial growths. They subdivide the changes met with as follows:

(1) True tumor shadows:

(a) Uncalcified tumors. These rarely throw a shadow except when they grow into one of the paranasal sinuses like the sphenoidal sinus.

(b) Calcified tumors, and true bone tumors. These are not to be confused with a calcified pineal gland, bilateral calcification of the chorioid plexuses, or with a median shadow due to calcification of the falx cerebri.

(2) Changes in the skull due to tumors:

(a) Changes resulting from general increase of intracranial pressure.
i. Enlargement of the skull as a whole.
ii. Separation of the cranial sutures.
iii. Atrophy of the inner table, showing markings corresponding to all the convolutions ("general convolutional atrophy").
iv. Destruction of the sella turcica or atrophy of the posterior clinoid processes.

(b) Local changes in the skull.
i. Local hypertrophies of the skull.
ii. Local enlargements of parts without destruction (*e. g.*, enlargement of the internal auditory meatus).
iii. Local atrophy of the skull.
iv. Local convolutional atrophy (especially in the frontal region).
v. Local sellar destruction.

(3) Vascular changes in the skull due to tumors:
(a) Enlargement of grooves due to arteries.
(b) Enlargement of the diploic sinuses.

True shadows must be distinguished from pseudoshadows; namely, light and dark areas most often seen in the temporal fossa or in the occipital or suboccipital region.

The most striking changes due to increased intracranial pressure seem to accompany subtentorial tumors (tumors of posterior fossa; cerebellar tumors); it is interesting that such tumors can destroy the pituitary fossa in a manner similar to the destruction accompanying sellar or supra-sellar tumors.

Local hypertrophies of the skull have most often accompanied endotheliomata or solitary tubercle.

### (*b*) *Focal Symptoms Due to Intracranial Growths*

The focal symptoms of intracranial growth may be absent (growths in silent areas), or when present may be due to (1) direct involvement of a non-silent area by the growth, or (2) indirect involvement by pressure of a growth in the neighborhood (neighborhood symptom), or at a considerable distance (distance symptom).

The focal symptoms to which brain tumors may give rise will be easily understood by consulting the subdivision on topical diagnosis. For convenience and quick orientation the following table may be consulted:

## *Table of Intracranial Growths (Brain Tumors, etc.)*

| Site of Growth in Brain | Commonest Types of Growth | Peculiarities of General Symptoms | Direct Focal Symptoms | Neighborhood and Distance Symptoms | Differential Diagnosis |
|---|---|---|---|---|---|
| *Lobus frontalis:* | | | | | |
| 1. Gyrus centralis anterior (motor area on right and left side). | Glioma; meningeal epithelioma; meningo-encephalitis syphilitica and tuberculosa; cysticercus. | | Cortical epilepsy; monoplegia; local paresthesia or bathyanesthesia. | | From pseudotumor cerebri (meningitis serosa; chronic intoxication; Reickard's acute or chronic brain swelling); dementia paralytica. From cerebral atherosclerosis with thrombosis. |
| 2. Left gyrus frontalis inferior (Broca's convolution). | Glioma; meningeal epithelioma; meningo-encephalitis syphilitica and tuberculosa; cysticercus. | | Slowly developing bradylalia and motor aphasia. | | |
| 3. Frontal lobe in front of anterior central gyrus (right or left). | Glioma; meningeal epithelioma; meningo-encephalitis syphilitica and tuberculosa; cysticercus. | Convulsions preceded by conjugate deviation. | Simple dementia; Witzelsucht; frontal ataxia. | Loss of contralateral abdominal reflex; fine homolateral tremor; psychoses. | |
| 4. Lobulus paracentralis (right or left). | Glioma; meningeal epithelioma; meningo-encephalitis syphilitica and tuberculosa; cysticercus. | | Monoplegia cruralis or spastic paraplegia; cortical cramps of leg muscles. | | |
| *Lobus parietalis:* | | | | | |
| 1. Gyrus centralis posterior (left or right). | Glioma; meningeal epithelioma; meningo-encephalitis syphilitica and tuberculosa; cysticercus. | | Bathyanesthesia; astereognosis; tactile agnosia; ataxia; apraxia. | Motor irritation or paralysis from compression of motor area in front of it. | |
| 2. Lobulus parietalis inferior (left side only). | Glioma; meningeal epithelioma; meningo-encephalitis syphilitica and tuberculosa; cysticercus. | | Alexia; optic aphasia. | Hemia-anopsia. | |
| *Lobus temporalis:* | | | | | |
| 1. Gyrus temporalis superior (left side only). | Glioma; meningeal epithelioma; meningo-encephalitis syphilitica and tuberculosa; cysticercus. | | Word-deafness; amnestic aphasia; paraphasia. | | Cerebral thrombosis. |
| 2. Uncus (right or left). | Glioma; meningeal epithelioma; meningo-encephalitis syphilitica and tuberculosa; cysticercus. | | Uncinate-gyrus fits; hallucinations of smell and taste; smacking of lips; tongue movements; pseudoreminiscences; anosmia. | | |
| 3. Other portions of left temporal lobe and of right temporal lobe. | Glioma; meningeal epithelioma; meningo-encephalitis syphilitica and tuberculosa; cysticercus. | Acoustic aura (in ear of opposite side) preceding convulsion or disturbance of consciousness. | | Hemiplegia or hemi-anesthesia (pressure on cerebral peduncle) (pressure on optic tract). | |

## *Table of Intracranial Growths (Brain Tumors, etc.)—Continued*

| Site of Growth in Brain | Commonest Types of Growth | Peculiarities of General Symptoms | Direct Focal Symptoms | Neighborhood and Distance Symptoms | Differential Diagnosis |
|---|---|---|---|---|---|
| *Lobus occipitalis:* | Glioma; lues; diffuse meningeal sarcomatosis. | Choked disk often absent. | Hemi-anopsia; hallucinations in one visual field; often no focal symptoms; in bilateral lesions optic agnosia. | | Vascular lesions. |
| *Interbrain:* 1. Region of basal ganglia and internal capsule. | Glioma; lues; bilateral tumors common. | | Gradual incomplete hemiplegia; hemi-chorea; hemi-athetosis; disturbance of mimic automatic movements; hemi - anesthesia; hemi-anopsia. | | Vascular lesions. |
| 2. Region of third ventricle. | Glioma; lues. | | Narcolepsy; tendency to comatose states. | Chiasm and hypophysis symptoms. | Dementia paralytica. |
| 3. Hypophysis (pituitary body). | Adenoma; cysts. | Choked disk often absent; headache often slight. | Diabetes mellitus or insipidus; acromegaly; enlarged sella turcica in radiogram; dystrophia adiposo-genitalis; menstrual disturbances; subnormal temperatures; disturbed tolerance for glucose. | Hemi-anopsia bitemporalis; unilateral or bilateral amblyopia; unilateral blindness with hemi-anopsia of the other eye; eye-muscle paralysis; exophthalmos; anosmia. | |
| *Corpus callosum:* | Glioma; lues. | Slight or absent. | Stupidity; sopor; conduction apraxia. | Bilateral hemiparesis, more marked on one side; cerebral nerves not compressed. | |
| *Midbrain:* 1. Corpora quadrigemina. | | | Pupillary paralysis; deafness; disturbance of optic-acoustic reflexes. | Tegmental symptoms (eye-muscle paralysis; movement ataxia; nystagmus; incoördination on standing and walking); hemi-anopsia (optic tract or lateral geniculate body); vaso-motor disturbances (cyanosis; asymmetry of body temperature on two sides); sexual disturbances. | |
| 2. Cerebral peduncle. (*a*) Tegmentum. | | | Eye-muscle paralysis (N.III and N.IV); disturbance of associated movement of the eyes (posterior longitudinal bundle); movement-ataxias and anesthesias (lemniscus); cerebellar ataxia (red nucleus and brachium conjunctivum). | | |
| (*b*) Pes pedunculi. | | | Hemiplegia alternans superior; intention tremor. | | |

## *Table of Intracranial Growths (Brain Tumors, etc.)—Continued*

| Site of Growth in Brain | Commonest Types of Growth | Peculiarities of General Symptoms | Direct Focal Symptoms | Neighborhood and Distance Symptoms | Differential Diagnosis |
|---|---|---|---|---|---|
| *Cerebellum:* | | Choked disk (90 per cent of cases), very early and bilateral; headache, occipital and cervical with tendency to rigidity of neck; often exaggeration of headache, vomiting and vertigo with change of position of head; vomiting nearly constant and early. | Sudden attacks of vertigo with cerebellar ataxia; Babinski's cerebellar asynergy and hemiasynergy; adiadochokinesis; homolateral hemi-ataxia with hypotony. | Compression of pons, medulla and cerebral nerves (facial neuralgia; anesthesia or paralysis); circulatory, respiratory and laryngeal symptoms; *Blicklähmung*; nystagmus; skew deviation; hemiparesis or paraparesis; forced attitudes and movements; hydrocephalus with compression of the chiasm and visual and hypophyseal symptoms; compression of olfactory lobes (anosmia); psychic disturbances absent until late. | |
| *Pons:* | | No choked disk. | Hemiplegia alternans; conjugate deviation of eyes and head toward the side opposite the tumor; dysarthria; dysphagia; unilateral or bilateral hemiplegia, anesthesia or ataxia; symptoms referable to N.V, N.VI, N.VII, N.VIII. | | |
| *Medulla oblongata:* | Cysticercus; lues; glioma. | Often slight or absent; sometimes optic atrophy instead of choked disk; headache occipital. | Symptoms referable to N.VIII, N.IX, N.X, N.XI, N.XII; deafness; dysphagia; dysarthria; hiccough; cardiac and respiratory disturbances; vaso-motor phenomena; glycosuria; diabetes insipidus; unilateral and bilateral paralysis of arm and leg; ataxia (cerebellar or lemniscal); head often held forward; course intermittent. | | |
| *Middle cranial fossa:* | Lues; sarcoma; neurofibroma of N.V; secondary carcinoma. | Choked disk early in carcinoma; absent in other tumors of this region except the tumors of N.V. | Involvement of N.II, N.III, N.IV, N.V, N.VI; loss of corneal reflex may be first sign. | Sensory and optic aphasia (compression of basal surface of temporal lobe). Sometimes neoplasm at angle of jaw. | |
| *Posterior fossa at base of skull:* | Tumors of N.VIII at cerebello-pontile angle (neurofibroma; sarcoma); sometimes bilateral. | Often absent or slight headache, choked disk and vomiting, sometimes severe. | Unilateral or bilateral symptoms referable to N.VIII (tinnitus, deafness, vertigo); N.V (loss of corneal reflex, anesthesia); N.VII or N.VIII; tetanuslike spasms. | Cerebellar ataxia; adiadochokinesis; movement ataxia; Blicklähmung; nystagmus; bulbar symptoms from compression of cerebellum, pons and medulla oblongata. | 1. From intrapontile tumors (choked disk absent; bilateral involvement of cerebral nerves early).<br>2. From tumors of cerebellar hemisphere (general symptoms pronounced; cerebellar symptoms earlier). |

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## 4. Symptoms of New Growths (Neoplastic or Inflammatory) Involving the Spinal Cord, its Meninges, or the Vertebral Column

Tumors may arise within the spinal cord itself (intramedullary tumors), in its membranous coverings (meningeal tumors), or in the mesoblastic structures surrounding the vertebral canal (vertebral tumors).

### (*a*) *Tumors Within the Spinal Cord*

(*Intramedullary Growths*)

The principal one is glioma. Occasionally, the cord is the site of a metastatic sarcoma or carcinoma. A gumma, or a tubercle, may arise in the gray matter of the cord; more often such a growth extends into it from the meninges.

#### i. Gliomatosis; Gliosis spinalis; Syringomyelia

Syringomyelia is most often due to degeneration of newly formed glia tissue, either of a true tumor (glioma) or of simple hyperplasia (gliosis), giving rise to tubelike cavities with beadlike bulgings, extending lengthwise in the spinal cord, especially in the gray matter, and sometimes, though not always, communicating with the central canal.

The condition is recognizable, clinically, by three sets of disturbances: (1) lower-motor-neuron lesions; (2) elective sensory disturbances; and (3) trophic and vasomotor disturbances.

The lower-motor-neuron disturbances consist of a chronic progressive spinal muscular atrophy with fibrillary twitchings and DeR. Since the cervical enlargement is most often affected, the distribution of the muscular atrophy often conforms to the Aran-Duchenne type, and gives rise to the "simian hand," or to the "claw hand." In addition, upper-motor-neuron lesions may gradually be added (spastic paresis).

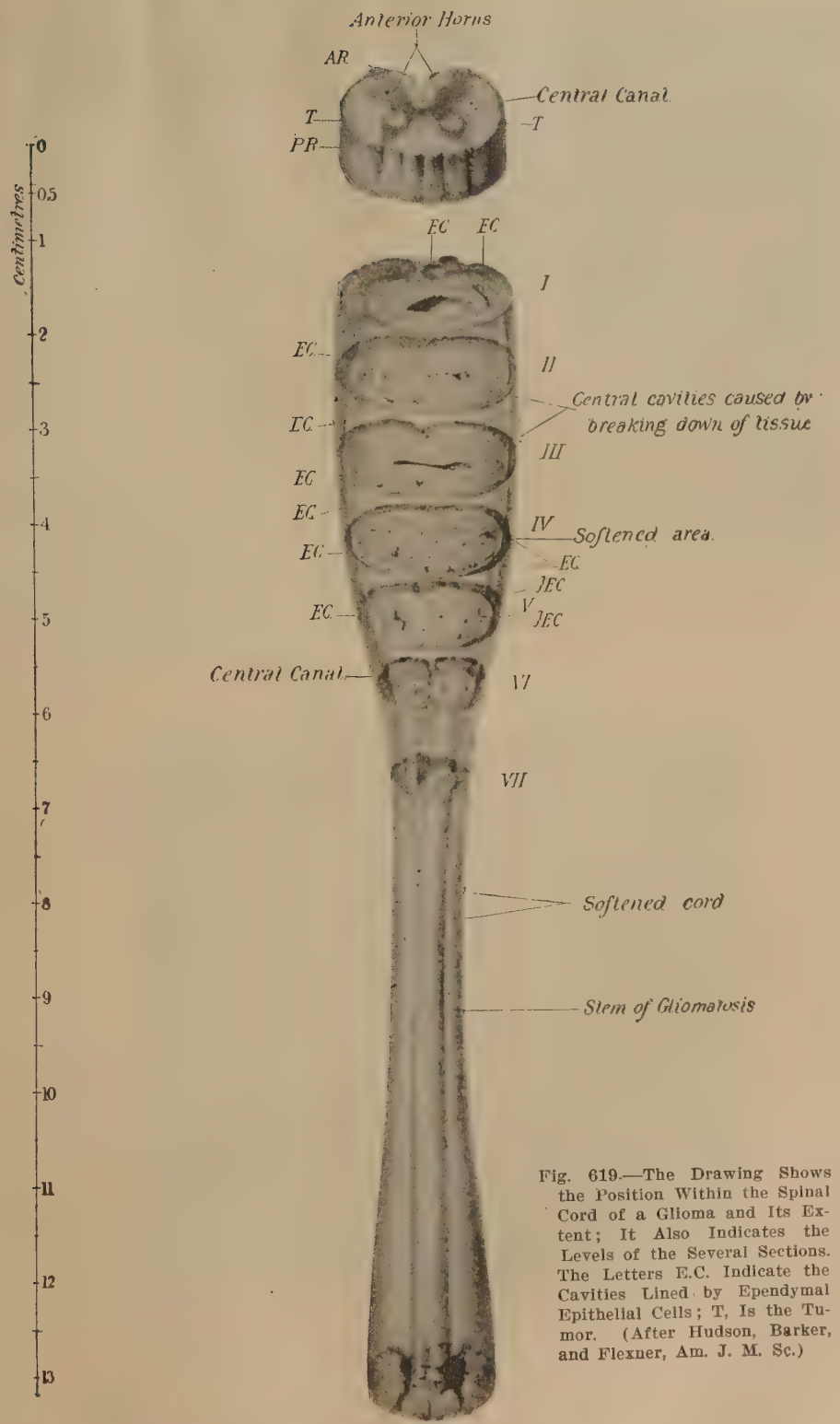


Fig. 619.—The Drawing Shows the Position Within the Spinal Cord of a Glioma and Its Extent; It Also Indicates the Levels of the Several Sections. The Letters E.C. Indicate the Cavities Lined by Ependymal Epithelial Cells; T, Is the Tumor. (After Hudson, Barker, and Flexner, Am. J. M. Sc.)

Fig. 620.—Syringomyelia. "Preacher's Hand" with Atrophy of Thenar and Hypothenar Eminence. (Med. Service, J. H. H.)

The elective sensory disturbances take the form of the so-called *syringomyelic dissociation,* or "posterior-horn type" of dissociation of sensibility, in which there is loss of pain sense and of the temperature sense, with intact sense of touch.

The trophic and vasomotor disturbances include panaritium, paronychia, urticaria, vesicle-formation, anomalies of sweat secretion, inflammation and deformation of bones and joints (osteo-arthropathies) involving especially the hands and feet, painless spontaneous fractures, kyphoscoliosis, etc. Sometimes the medulla oblongata is invaded, giving rise to hemi-atrophy of the tongue, paralysis of the N. recurrens, and oculopupillary symptoms (in the domain of the cervical sympathetic).

Fig. 621.—Syringomyelia. "Main Succulente." (Med. Service, J. H. H.)

Three types of the disease have been distinguished, according as the motor, sensory or trophic disturbances predominate.

**Differential Diagnosis.**—Each of the three types may give rise to symptoms resembling other diseases. We must especially distinguish:

1. The predominantly motor type from: (a) *amyotrophic lateral sclerosis,* (b) *spastic spinal paralysis,* and (c) the *spinal type of progressive muscular atrophy.*

2. The predominantly sensory type from: (a) *pachymeningitis cervicalis hypertrophica,* (b) *hysteria,* and (c) *hematomyelia.*

3. The predominantly trophic type (the so-called "Morvan's syndrome," in which analgesia and thermanesthesia, with slight tactile anesthesia, are combined with panaritium and cutaneous vesicles), from *lepra mutilans.*

In syringomyelia the elective sensory paralyses (analgesia and thermanesthesia) are due to lesions of the posterior horn, the muscular atrophies to lesions of the anterior horn, the trophic and vasomotor disturbances to lesions of the gray matter, especially the lateral horn. The disease is thus predominantly due to lesions of the gray matter. When spastic symptoms develop, they are an indication of extension to the white matter of the lateral funiculus; when ataxia and tactile anesthesia complicate the picture, they indicate an extension to the posterior funiculi.

### (*b*) *Tumors External to the Spinal Cord*

(*Extramedullary Growths*)

The extramedullary tumors are divisible, as we have already learned, into those developing within the spinal canal (meningeal tumors) and those arising in the spine itself (vertebral tumors).

#### i. Meningeal Tumors

Meningeal tumors and inflammatory nodules (sarcoma, endothelioma, fibroma, gumma, tubercle) vary in size from that of a pea to that of an olive or even larger, often extending two inches, or more, in a vertical direction. The growth is usually slow (except in lues), leading to gradual compression of the cord, the compression often injuring the gray matter more than the white, and sometimes the opposite half of the cord more than the adjacent half.

Meningeal tumors may occur at any level, though they are most common in the thoracic region, on account of its greater length. They are also common in the cauda equina, and in the region of the cervical enlargement.

The clinical phenomena appear in three stages: (1) the *stage of root symptoms* (unilateral or bilateral segmental neuralgia, sometimes

combined with hyperesthesia), lasting for several months or even for two or three years; (2) the *stage of hemilesion of the cord* with Brown-Séquard syndrome (*q. v.*); and (3) the *stage of compression of the whole cord* with corresponding bilateral paralyses, anesthesias and sphincter disturbances below the level of the lesion.

Localization in the cervical, thoracic and lumbar regions, or in the cauda equina, can be made by application of the principles discussed under Topical Diagnosis. We should try to determine not only the segmental level of the tumor, but, also, whether it lies upon the anterior, or posterior, surface of the cord.

**Differential Diagnosis.**—Accurate diagnosis is here most important on account of the possibilities of surgical therapy. In typical cases, there is no difficulty. In atypical cases, a tumor may be confused with (1) *lues spinalis* (quick development, marked oscillation of symptoms, lesions at several levels, Wassermann positive, therapeutic test); or (2) *multiple sclerosis* (absence of root symptoms, coëxistence of cerebral symptoms).

It is especially in multiple neurofibromata, and in angiomata of the nerve roots, or meninges, that confusion with lues, or with multiple sclerosis, is likely to occur.

Extramedullary growths are usually easily differentiated from (3) *intramedullary growths* (gliomata) in that the latter (a) rarely cause root pains; (b) extend in the vertical direction rather than in the transversal direction; (c) throughout follow a course that is much more chronic and insidious; (d) cause anesthesias that are elective and segmental in topography, and do not have the topography of anesthesias due to hemilesion.

In applying the principles of topical diagnosis for the determination of the segmental level we pay especial attention to:

1. The level of radicular pains, of paresthesias or of anesthesias.
2. The levels injured as indicated by the loss of reflexes.
3. The levels directly injured in their anterior horns, as shown by degenerative muscular atrophies with DeR.
4. The upper level of a hemilesion (upper limit of contralateral anesthesia in Brown-Séquard's syndrome).
5. The levels indicated by x-ray examination, or by tenderness of spinous processes on palpation, or on application of a hot sponge.

### ii. Vertebral Tumors

Besides true tumors (primary or secondary sarcoma, metastatic carcinoma, osteoma, etc.), caries, gumma, and echinococcus cyst have here to be considered. The distinction of these vertebral growths from meningeal growths, on the one hand, and from intramedullary tumors, on the other, is usually possible by a consideration of certain of their characteristics: (1) the palpable or visible localized deformities of the spine; (2)

the findings on x-ray examinations; (3) tenderness of the spine and interference with its movements; (4) the rapid and bilateral involvement of the nerve roots and of the spinal cord, once these structures are attacked; (5) the existence of a primary tumor elsewhere, since vertebral tumors are often secondary; (6) the occurrence in advanced life, and in cachectic persons.

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## 5. Multiple Neurofibromatosis; von Recklinghausen's Disease

**Definition.**—A neoplastic disease affecting more or less extensively different parts of the peripheral nervous system and characterized by the development of multiple fibromata in the nerves of the skin and other

A B

Fig. 622.—Von Recklinghausen's Disease. A, Anterior View; B, Posterior View. (Med. Service, J. H. H.)

nerves, causing cutaneous and subcutaneous tumors (mollusca fibrosa), anomalies of pigmentation, and elephantiasislike formations.

**Symptoms.**—There may be only a few tumors in the skin or there may be hundreds of them. They vary in size from that of a small point to that of a hen's egg. They are most numerous upon the trunk, but they occur

also upon the extremities. The subcutaneous tumors are spindle-shaped. I saw one case in which the abdominal wall contained a number of rather large tumors of this type. When there is a diffuse fibromatosis of several nerves or of a nerve plexus, the condition is known as "plexiform neuroma," whereas a bundle of racemose nodular masses forming an isolated tumor not intimately connected with a nerve trunk or a plexus is called a "racemose neuroma" (*Rankenneurom* of von Bruns). The so-called "elephantiasis neuromatosa" or pachydermatocele occurs most often on the feet, legs, hips, genitals, neck or face; it is usually congenital, and has a slow, painless evolution.

Abnormal pigmentation can nearly always be made out, in the form of brown spots, naevi, or diffuse discolorations of the skin. Sometimes spots with less pigment than normal are also visible over the skin. Angiomata of the skin are so often present that Harbitz regards their occurrence as a true feature of the disease.

The patients often present psychic anomalies (apathy, imbecility). Congenital defects and malformations (skeletal, genital) may be found in some cases. The *formes frustes* of the disease are very common. The disease is always congenital, often hereditary and sometimes familial (Feindel).

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## J. The Neuroses and the Pyschoneuroses

Under this heading we may consider the diagnosis of:

(1) Hysteria; (2) the neurasthenic and psychasthenic states; (3) hypochondriasis; (4) the traumatic neuroses; (5) epilepsy; (6) mi-

graine; (7) the tic disease; (8) paramyoclonus multiplex; (9) occupation-neuroses; (10) Sydenham's chorea; (11) Huntington's chorea; (12) paralysis agitans; (13) myasthenia gravis pseudoparalytica; (14) periodic family-paralysis; (15) periodic oculomotor-paralysis; (16) myotonia congenita; (17) amyotonia congenita; (18) dystonia deformans progressiva.

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## 1. Hysteria

**Definition.**—A disease characterized by an abnormal mental state, in which there is a disproportion between affective reactions and the stimuli that give rise to them, slight stimuli often causing a violent emotional reaction, a similar stimulus at other times having no effect; in this disease, too, remarkable motor, sensory, vasomotor and secretory disturbances of "psychogenic" origin are met with; the suggestibility of the patient is heightened (both autosuggestion and heterosuggestion); the sudden transformations of the emotional states and the moods, as shown in caprice, are very characteristic.

**Etiology.**—The disease is much more common in females than in males. It begins to manifest itself usually in adolescence, sometimes in childhood. Most patients have a distinct neuropathic, or psychopathic, predisposition. Provocative causes are psychic traumata (fright, anxiety); a pathological example (mother, comrade); sexual traumata, intoxications, and physical traumata.

**Symptoms.**—These are protean in their variability. They may be divided into (1) the so-called somatic stigmata, and (2) the psychic manifestations.

Somatic Stigmata.—These include:

(a) The *globus hystericus,* a feeling of constriction in the neck, or of a lump in the throat, which "cannot be swallowed," usually associated with loss of the pharyngeal reflex.

(b) The *clavus,* or pain in the region of the large fontanelle, described as resembling a "nail being driven in," or as though "worms were creeping about" there.

(c) *Hysterical paralyses* (hemiplegia, monoplegia, aphonia, astasia-abasia, ptosis, etc.).

(d) *Hysterical contractions,* including retention of urine.

(e) *Hysterical hyperesthesias,* including:

(i) The so-called *spinal irritation,* or tenderness on tapping the spine; (ii) the so-called *ovarian irritation,* or tenderness on pressure in the region of the ovary; and (iii) various *hyperesthetic zones* in the body.

(f) *Vasomotor* and *secretory lability,* as expressed in:

(i) Dermographia; (ii) hot and cold flushes; and (iii) localized disturbances of sweating.

(g) The *grand hysterical attacks,* in which patients, without injuring themselves, sink down and assume, and maintain for some time, remarkable attitudes, such as the arc of a circle, or various pathetic, or theatrical positions (*attitudes passionelles*), or exhibit wild, rotating movements (*clownism*). Such attacks are easily distinguished from epileptic seizures, in that the patients do not injure themselves, do not bite the tongue, and there is, as a rule, no postconvulsive sleep, nor are the pupillary reactions lost; the whole attack can be terminated, generally, by a dash of cold water.

(h) *Rudimentary hysterical attacks,* including hysterical laughing, crying, coughing, hiccough, cramps in certain muscle groups, etc.

(i) *Hysterical anesthesia.*—This may affect one extremity, one half of the body, or two extremities simultaneously, becoming ever more marked as it is more attended to. Often the anesthesia has a topography corresponding to areas of skin covered by certain articles of clothing (gloves, chemise, drawers, stockings).

(j) Exaggerated reflexes with false ankle-clonus may sometimes be present.

The relation of these somatic stigmata to emotional states is characteristic.

Psychic Stigmata.—The principal mental stigmata are:

(a) The disproportion of affective states to the stimuli arousing them.
(b) Pathological lability of mood.
(c) Fallacies of memory.
(d) Ideas of reference and of lack of consideration.

(a) *The Disproportion of Affective States to the Stimuli Arousing Them.*—The patients are abnormally irritable, and slight annoyance may lead to explosive behavior. It sometimes seems as though the smallest stimulus excited the greatest reaction, whereas in real difficulties, the hysterical may have a good grip on themselves. A single well-meant word

may precipitate an attack and give rise to convulsions and twilight states. This pathological irritability is more intense at the menstrual periods, at the menopause, and during pregnancy.

(b) *Pathological Lability of Mood.*—The hysterical patient may be happy, jolly and easily accessible one moment, and the next moment, without any apparent reason, become the reverse—irritable, suspicious, sullen. No one can foresee the patient's mood. It is bizarre, oscillatory, incalculable.

(*c*) *Fallacies of Memory.*—Hysterical patients often seem unable to distinguish what they remember, from what they imagine. They are incapable of objective report, owing to their lively fancy and pathological combining power. They are thus thought by their comrades to be liars, but the *hysterical lie* is a pathological phenomenon due to faulty reproduction, or to transformation of memories—the so-called *pseudologia fantastica,* or *mythomania.* Hysterical patients, sometimes, have complete *amnesia* for certain periods; or the amnesia may concern only certain persons, or events.

(d) *Ideas of Reference and of Lack of Consideration, Due to Personal Hypersensitiveness.*—In the hysterical character, these psychic stigmata are combined with a diminution of the capacity for ethical ideas. The patients refer to themselves, comments or acts not at all so intended. Their feelings are easily hurt; they believe that they are "misunderstood"; they think that others do not pay them the attention that is their due, or that they intentionally slight them. These ideas of reference and slight paranoid symptoms do not, however, attain to anything like the systematic development seen in outspoken paranoid states.

*Other Hysterical Phenomena.*—Many hysterical patients suffer from *psychogenic bodily disturbances.* They may be unable to eat, or they vomit almost constantly (*anorexia nervosa*); or the abdomen may be continuously distended with gas (*hysterical meteorism*); or the urine may be retained for days or weeks, unless catheterized (*hysterical retention*). Many such patients think themselves pregnant (*pseudocyesis,* or *hysterical pregnancy*).

More *severe mental disturbances* sometimes develop on an hysterical basis. There may be transitory disturbances of consciousness (*hysterical twilight states, somnambulisms, trances*). The hysterical twilight states appear suddenly and often take the form of protracted "passionate attitudes" after an hysterical attack; or they may appear instead of an attack (as an *equivalent*). The patients are confused, behave like children, and often make one think of simulation, the condition lasting for hours, days or weeks (*Ganser's symptom-complex*). Somnambulisms represent one form of the twilight state. The patients often go through the movements that correspond to some previous emotional experience.

In hysterical trances, or lethargic states, the patient may sleep for

days, weeks or months, sometimes pale like a corpse, sometimes with rosy cheeks.

In severe cases, hysterical insanities develop, sometimes of the paranoid type, sometimes of the erotic type, sometimes of the exaggerated philanthropic type.

Hysterical symptoms are often worse at the menses and especially at the menopause or during pregnancy. At such times, hysterical patients are difficult to live with. They have been compared to an explosive mixture.

Astásia-abasia.—This symptom is usually of hysterical origin, though it may also be met with in psychasthenic states.

Standing and walking are difficult, or impossible. When the patient lies down, no disturbance of motility, sensibility, or coördination, can be made out. Some patients, who cannot stand or walk, can go upon all fours or can swim. The condition is commoner in women than in men, and in young people than in the old.

It must be differentiated (1) from cerebellar ataxia, and (2) from vestibular disease.

I saw one such patient who had astasia-abasia under ordinary circumstances, but could free himself of it, entirely, by drinking a pint of whiskey. As soon as the effects of the alcohol wore off, he again showed the symptom. In his case, I regarded the condition as a phobia of psychasthenia. A closely related symptom is the inability to sit (*akathisia*); this must also be a phobia.

There is, however, a form of astasia-abasia that is not uncommon in old people in association with psychaesthenic states and early mental deterioration. Boggs and Pincoffs have seen a number of such cases at Bay View Hospital and Pic treats of the condition at some length in his *Maladies des Vieillards.*

Akinesia algera.—In this condition, first described by Möbius, there is immobility on account of pain, although no cause for the pain is discoverable. It occurs in psychoneurotic states (psychasthenia, hysteria). The symptom is probably to be regarded as an hallucination in the domain of the pain sense. Some of these patients during the attacks of pain manifest tachypnea and tachycardia (Oppenheim). Allied disturbances are (1) the so-called *dysopsia algera,* in which vision is interfered with, because on looking at objects the patient has pains in the eyes and head; (2) *atremia,* in which the patient cannot leave the bed because standing, walking and sitting cause pain; and (3) *aphagia algera,* in which the patient refuses to take food because it gives him pain.

The condition should be differentiated from (1) organic conditions causing pain, and (2) the neurotic symptoms of Graves' disease.

**Diagnosis of Hysteria.**—The recognition of hysteria is usually easy

through the characteristic stigmata and through the exaggerated, often theatrical, character of the mental symptoms and the capricious, oscillatory course (See Epilepsy).

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## 2. Neurasthenic and Psychasthenic States

In these states there is an increased irritability of the nervous system with diminished capacity (irritable weakness).

The *somatic symptoms* consist of heightened irritability, and especially fatigability of all the functions mediated by the brain, the spinal cord and the sense organs, and by the organs under the domination of the autonomic nervous system (circulatory, digestive and sexual apparatus).

On the *psychic side,* the patients complain of various uncomfortable feelings—depressions, anxieties, fears, etc. The tendency at present is to classify the cases in which the somatic signs are the more prominent as neurasthenic states, and those in which the psychic signs are the more prominent as psychasthenic states.

**Etiology.**—There is nearly always an inherited neuropathic predisposition, often with stigmata of degeneration, though some patients with good heredity become neurasthenic or psychasthenic owing to severe psychic or somatic injury (physical and mental over-exertion; struggle for existence, responsibilities, insufficient sleep, exercise or food); exhausting diseases (digestive, venereal, general infectious, or metabolic); excessive use of alcohol and tobacco, sexual excess. The beginnings of

dementia precox, of a manic-depressive psychosis, and of a Grave's disease are often treated as neurasthenic states.

**Symptoms.**—In the foreground stand pathological fatigability and irritability. Headache, vertigo and insomnia are common symptoms. Nervous asthenopia, hyperesthesia acoustica, neuralgic pains, paresthesias, are often complained of. A feeling of weakness in the limbs on the least exertion, and tremor are common.

Objectively, the reflexes are often exaggerated, though the pupils are normal, and speech, except for hesitation or slight stuttering, is unaffected.

On the psychic side, fatigue on the least mental exertion, and abnormal irritability of mood, are the characteristic symptoms. Inability to concentrate attention, or to pursue steadily a chain of thought, except when the patient is dealing with his own symptoms, is common. Neurasthenic patients complain of lack of energy, of indecision, of fears and of abnormal impulses (*vide infra*). These psychic symptoms are most pronounced in the so-called psychasthenic states, characterized by periods in which there is a high grade of indecision or doubt (*folie de doute*), and in which the patients are plagued by feelings of anxiety (precordial, cephalic or general), fears of people (anthropophobia), of places (agoraphobia), of being shut in (claustrophobia), of incurable disease or insanity (nosophobia), of contamination with unclean, or infectious objects (mysophobia), or of contaminating what they touch (*délire de touche*).

Many patients have outspoken obsessions or imperative ideas; the best description of these states is that given by Raymond and Janet.

Sometimes the patients suffer from an imperative impulse to speak obscenely (copralalia), or to echo what they hear (echolalia), or that they must perform certain acts in certain ways. Some of them suffer from an interrogative mania, asking themselves continuously foolish questions regarding ordinary things in the environment. These symptoms appear against the will of the patient and are recognized by him as abnormal, as something foreign to him, which he tries vainly to resist.

**Differential Diagnosis of Neurasthenic and Psychasthenic States.**—We must carefully exclude (1) *organic diseases* (dementia paralytica; multiple sclerosis, tumor cerebri, cerebral atherosclerosis, Graves' disease, etc.), (2) *psychoses* (manic-depressive insanity, paranoia, dementia precox), and (3) *other neuroses* (hysteria, myasthenia gravis).

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## 3. Hypochondriasis

Here the patient's attention is continuously occupied with the condition of his own body or mind, his pathological feelings giving rise to hypochondriacal anxieties, fears and ideas. Sometimes these hypochondriacal ideas become fixed beliefs in which the patient cannot be shaken (true hypochondriacal delusions). In many cases, these hypochondriacal states appear to be dependent upon abnormal visceral sensations.

The hypochondriacal form of neurasthenia is separable from the hypochondriacal ideas (1) of *manic-depressive insanity* (ideas secondary to the depression and accompanied by ideas of sin and psychomotor retardation); (2) of *chronic paranoia* (ideas of disease produced artificially by enemies, combined with grandiose ideas, and ideas of persecution, in a system); and (3) of the *catatonic forms of dementia precox* (patients non-suggestible and apathetic, negativistic and, later, hallucinant), and (4) of *dementia paralytica* (specific, somatic and psychic signs).

## 4. The Traumatic Neuroses

Here we have to deal with psychoneurotic states closely related to hysteria and to neurasthenia, especially of the hypochondriacal type.

**Cause.**—A physical, or psychic, trauma, acting upon a predisposed nervous system (fright, sexual trauma, railway accidents, automobile acci-

dents, and the like). Fear of loss of position or health, financial worries, and especially the possibility of legal damages ("ideas of covetousness"), often play a part.

**Symptoms.**—The symptoms are very variable, including those of neurasthenia (fatigability, irritability, anxiety, lacrimation, headache, vertigo, vasomotor disturbances, tremor), those of hypochondriasis (pathological self-observation, mental depression, apathetic facial expression), and those of hysteria (anesthesias or hypesthesias of hysterical type, contraction of the visual fields, twilight states with irrelevance, suggesting simulation). In many cases, there are evidently slight organic lesions present (commotio cerebri et spinalis), manifest in objective disturbances of motility and sensibility. It is sometimes difficult to decide in how far the sensory, motor and reflex symptoms are organic, and in how far "psychogenic" in origin. The latter usually arise first exclusively, or predominantly, on the side that was injured.

**Differential Diagnosis.**—1. From *simulation*, which is much rarer than is commonly believed (absence of exaggeration of reflexes, of increased mechanical excitability of muscles and nerves, of fibrillary twitchings, of atrophies, of pupillary differences, and of typical contraction of the visual fields).

2. From *hematomyelia* (elective dissociation of sensibility).

3. From *caries of the spine* (*q. v.*).

4. From *brain abscess* (*q. v.*).

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## 5. Epilepsy

*(Falling Sickness, Morbus sacer)*

A condition characterized by sudden peculiar disturbances of consciousness, associated, in typical cases, with convulsive seizures (epileptic or epileptiform convulsions), or with the occurrence of certain signs (epileptoid signs) that permit of the recognition of an epileptic constitution of the brain.

Epilepsy may be (1) *genuine* or *idiopathic* (no cause demonstrable); (2) *symptomatic* (due to coarser organic lesions of the brain, like tumors, abscesses, trauma, hydrocephalus, etc.); or (3) *reflex* (due to peripheral irritation of adenoids, ear-diseases, tight prepuce, intestinal worms, etc.).

Some assume that the so-called idiopathic epilepsy depends upon a progressive proliferation of the glia, and that this "epileptic alteration" is the cause of convulsive cerebral response in various forms of intoxication, circulatory disturbance, etc. The so-called *senile epilepsy* is nearly always dependent upon atherosclerosis. *Late epilepsy* or *epilepsia tarda,* (beginning after thirty) is often due to lues, or to brain tumor.

**The Typical Epileptic Fit.**—This is often preceded by an *aura,* which may be (1) some form of hallucination (visual, auditory, olfactory, gustatory, kinesthetic), (2) a subjective feeling of anxiety, or (3) some vasomotor phenomenon. The fit itself is divisible, in typical cases, into five stages:

1. The patient *cries* out and suddenly *falls unconscious,* often injuring himself severely;

2. The voluntary musculature undergoes *tonic spasm,* often in opisthotonos, with pallor of the face, giving way later, on account of respiratory spasm, to lividity and conjugate deviation of the eyes and head, with contraction and rigidity of the pupils and cessation of breathing (fifteen to thirty seconds).

3. The stage of *clonic convulsions,* involving most of the muscles of the body, including those of respiration, as well as the muscles of the eyes and head, and lasting several minutes. The tongue is often bitten. The patient froths at the mouth.

4. The stage of *stertorous breathing,* with complete analgesia and coma.

5. The stage of *terminal sleep,* so sound that it may be scarcely possible to waken the patient during the first half hour, and, when it is possible to waken him, he is confused and dull.

The reflexes are abolished during the attack. Urine is frequently, and feces occasionally, passed involuntarily.

In less typical attacks one or more of the stages of the type described may be absent, and instead of complete unconsciousness with subsequent amnesia, there may be only an altered state of consciousness. The number of epileptic seizures varies; some patients are attacked daily, others only once in two or three years. Very frequent attacks are known as *serial* epilepsy, or, where fit follows fit for hours and days, we speak of *status epilepticus* (see also Cerebral Fits).

**So-called Epileptoid Signs.**—These include (1) the so-called minor attacks (*petit mal*), (2) epileptic vertigo, (3) epileptic nightmare (*pavor nocturnus*), (4) epileptic bed-wetting (*enuresis*), and (5) epileptic anxiety attacks.

In petit mal, instead of a typical fit, there is only momentary loss of consciousness with pallor, and perhaps slight twitchings of single muscles in the face, or of an extremity, without a fall.

In epileptic vertigo, the patient, without apparent cause, is attacked suddenly with transitory vertiginous feelings, often combined with pallor, but without loss of consciousness, or actual fall. The vertigo may be associated with tachycardia or bradycardia, flushing of the face, dilatation of the pupils, sweating and headache.

The diagnosis of epilepsy depends upon the presence of outspoken epileptic fits or upon the presence of several of the epileptoid signs.

**Psychic Complications of Epilepsy.**—In addition to the unconsciousness, and the alterations of consciousness above mentioned, epileptics may be the victims of (1) epileptic twilight states; of (2) a progressive degenerative change in the character and of the mental individuality (epileptic character), or of (3) complicating psychoses.

Epileptic Twilight States.—These may precede, or follow, the attacks (pre-epileptic or postepileptic twilight states); or they may take the place of an attack (epileptic equivalent). Such twilight states may last for minutes, hours, days, weeks, or even months. In them, the patients often undertake long journeys (ambulatory automatism, poriomania, epileptic fugues). During the twilight state, the patients often repeat the same act in precisely the same way, not unlike the acts of the hysterical somnambulist, but the epileptic's acts are often violent (murder, incendiarism, rape, etc.). Some of the patient's acts are simple and natural, whereas others are strange or violent.

The epileptic character results from a progressive change in the personality. This sometimes comes on quickly, but its advance is generally slow. It is characterized by great irritability, outspoken ethical defects, violent egoism, and lying. The patients gradually develop a tendency to violence under excitation, and may perform criminal acts. The intellect also suffers (forgetfulness, enfeeblement of judgment, dementia).

Epileptics are very intolerant to alcohol, and small quantities of it may be responsible in them for extremely violent and dangerous acts.

Psychoses Complicating Epilepsy.—Epileptics seem to be especially liable to the development of psychoses of various forms (maniacal, melancholic, paranoiac, catatonic).

**Differential Diagnosis.**—Attacks of *grand mal* and of *petit mal* rarely offer difficulty, though the decision as to whether the epilepsy is idiopathic, symptomatic, or reflex may be hard to arrive at. Accurate examination and long observation may sometimes be necessary. A single convulsive seizure does not justify the diagnosis of epilepsy.

It is important to differentiate epilepsy (1) from *convulsions in early childhood;* (2) from *hysteria;* (3) from *uremia, eclampsia* and *other forms of intoxication.*

In differentiating hysteria the history of the case as regards biting of the tongue and incontinence of the sphincters in attacks, the presence of scars on the tongue, or head, the stupidity of epileptics as contrasted with the brightness of hysterics, are helpful points. Hysterical attacks may occur without prodromata, as a result of emotion. Hystericals are accessible to suggestion but are uninfluenced by bromids. The epileptic attack is often preceded by an aura, and is much shorter than an hysterical attack. The epileptic convulsions rarely last longer than ten minutes, while hysterical attacks usually continue longer than fifteen minutes. The pupils in hysteria are unaltered, and the face is rarely pale.

*Petit mal* must be differentiated from *simple syncope* (feeble pulse, coma temporary and less deep, absence of all symptoms of motor irritation).

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## 6. Migraine

### (*Hemicrania, Sick Headache*)

The condition is characterized by periodic attacks of headache, usually unilateral, and often associated with nausea, vomiting and vertigo. The attacks last from a few hours to one or several days. Various prodromata are complained of (dull feeling, drowsiness, depression, pressure in the head, unusual hunger or thirst, etc.). During the attack, the

scalp, or the region of the upper cervical ganglion of the sympathetic, may be tender on pressure, and the patient is abnormally sensitive to light, sounds and smells. He lies in a darkened room, and suffers from complete anorexia. There may be vomiting, or diarrhea; sometimes there is salivation and polyuria. The attack often ends in a sleep, from which the patient awakens quite well. Some patients have weekly or monthly attacks; others suffer at longer intervals.

The patients sometimes show symptoms of irritation of the cervical sympathetic (*hemicrania sympathicotonica*); others show symptoms suggestive of paralysis of the same (*hemicrania sympathicoparalytica*).

In still other patients, eye symptoms are prominent (*hemicrania ophthalmica, migraine ophthalmique*). The onset of the headache in these is heralded by peculiar visual disturbances. A light-point appears in the visual field, which spreads or assumes a zig-zag figure (fortification scotoma); in some instances there is partial or complete hemi-anopsia, more rarely, actual temporary blindness, lasting for a few minutes, or even for half an hour. Now and then a patient is temporarily aphasic. Paresthesia, monoparesis or cerebellar symptoms may accompany the attack.

Hemicrania is often associated with other neuroses (neurasthenia, hysteria, epilepsy, writer's cramp). Some patients appear to suffer from hemicranic equivalents (vertigo, cardialgia, gastric hyperacidity, topoalgia, hemiparesis),

The view that hemicrania depends upon local angiospasms causing focal symptoms in the brain is favored by some. Others assume recurring auto-intoxications, refraction anomalies (Gould), nasal disease, etc., as the cause.

**Differential Diagnosis.**—Usually easy, especially if attacks begin in youth, and one parent has previously suffered from them. Care must be taken to exclude (1) *tumor cerebri,* (2) *uremia,* (3) *glaucoma,* and (4) *meningitis serosa.*

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## 7. The Tic Disease

A tic is a coördinated movement that has become imperative; it may correspond to a movement of a reflex, defensive or expressive type. The movement is not brought about by an external stimulus, or by an adequate psychic process, but by an irresistible internal impulse to movement, which arises in consciousness and makes the patient uncomfortable until the movement is performed. It is usually brief, often violent, and it is always performed in precisely the same way. The disease may be limited to a single movement (localized, or isolated, tic); or it may be characterized by a multiple series of tics; or, as in the disease of Gilles de la Tourette, there may be a generalized tic (*maladie des tics convulsifs*).

**Isolated Tics.**—As examples may be mentioned the facial tic, and the tics representing specific acts (sucking tic, licking tic, biting tic, scratching tic, gritty tic, etc.).

**Generalized Tic.**—The disease usually begins with some form of facial tic (blepharospasm, distortion of the mouth), or with a cervical tic. Later, tics involving the extremities appear (grabbing nose, pulling chin or beard, throwing head to side, hand-clapping, foot-stamping, teeth-gritting, etc.). The movements undergo stereotyped repetition. Obscene words may be frequently repeated (coprolalia). Some patients exhibit symptoms of command-automatism (echolalia, echokinesis, *q. v.*). Obsessions sometimes appear. The disease is, as a rule, progressive. In some instances, it appears to be part of a psychasthenic state; in others, of a dementia precox.

**Differential Diagnosis.**—(1) From *Sydenham's chorea* (movements not systematic, absence of command-automatism, relation to tonsillitis or rheumatism); (2) from *hysteria* (sudden origin, suggestibility, absence of coprolalia); (3) from *paramyoclonus multiplex* (*q. v.*); and (4) from *athétose double* (*q. v.*).

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[Note.—See also references under Tics in Part XII, Sect. i.]

## 8. Paramyoclonus multiplex

(*Myoclonia, Polyclonia*)

This condition is characterized by clonic contractions involving chiefly the muscles of the extremities and trunk, the face being slightly, if at all, affected. The contractions cause short quick jerks, not involving synergistic muscle groups, and varying in number from a few to a hundred per minute. Single muscles (for example, the M. brachioradialis) that cannot be voluntarily contracted by themselves, may be affected. The muscles especially prone to involvement are: (1) M. brachioradialis; (2) M. biceps; (3) M. trapezius; (4) M. quadriceps femoris; and (5) M. semitendinosus.

The contractions disappear in sleep. The deep reflexes are exaggerated. All other neural functions are normal.

A family form of the disease has been described (Unverricht), in which the patients are often epileptic. Occasionally the patients deteriorate mentally (*dementia myoclonica*). Males are more often affected than females.

**Differential Diagnosis.**—(1) From *hysteria;* (2) from *epilepsy;* (3) from *chorea chronica;* (4) from the *tic disease.*

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## 9. Occupation Neuroses

Persons of various occupations are prone to a disturbance of coördinated muscular innervation for certain special skilled movements that pertain to their occupations, the muscles concerned responding to the will for all other movements. The commonest form is so-called "writer's cramp," but there seem to be almost as many occupation neuroses as there are occupations (telegrapher's, teller's, cigarmaker's, watchmaker's, dancer's, pianoplayer's, tennis player's, seamstress's, 'cellist's cramp, etc.).

### (*a*) *Writer's Cramp*

(*Mogigraphia, Graphospasm*)

This develops most often in psychoneurotic patients (persons suffering from neurasthenia, epilepsy, psychasthenia, hemicrania, neuralgia, etc.), and in those who have been improperly taught to write and who, on this account, use unnecessary force, and overtax the small muscles of the hand. The disturbance develops gradually; the first thing noticed is an abnormal fatigability on writing; later, the power over the pen grows less and less, and a feeling of cramp in the muscles is complained of, especially in the flexors of the thumb and the index finger; other muscles are, often, also involved. Pain, from now on, accompanies attempts to write; the writing becomes irregular, sometimes almost illegible, especially when the writer is under observation. Spastic, paralytic, and neuralgic forms have been described. On physical examination, the nervous system may be otherwise negative, except for the presence of psychoneurotic signs.

**Differential Diagnosis.**—We must distinguish writer's camp from: (1) *agraphia;* (2) *paralysis agitans* (miocrographia); (3) a developing *hemiplegia;* (4) a *tabetic ataxia* beginning in the upper extremities; (5) the intention-tremor of *multiple sclerosis;* and (6) *dystonia musculorum progressiva* (*q. v.*).

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## 10. Chorea minor

*(Sydenham's Chorea, St. Vitus's Dance)*

Children are chiefly affected (5 to 15), though chorea may occur at any age, the condition in adults being met with in pregnant women (chorea gravidarum), in acute articular rheumatism, or in endocarditis.

**Symptoms.**—After indefinite prodromata (irritability, tendency to whine, restlessness, clumsiness, "naughtiness"), the involuntary, irregular jerking movements, which are exaggerated by excitement, appear, often affecting the whole body, or sometimes limited to one side (*hemichorea*). The movements cease in sleep, except in rare cases (*chorea nocturna*). They resemble voluntary movements, but differ from them in that they are purposeless, and in that there is a constant change in the form and direction of the movement. There is an absence, too, of the ordered cooperative activity of the antagonists with the chief agonists and synergists. [For a full analysis of the choreatic disturbances of motility, see section on Examination of the Motility.]

Fig. 623.—Chorea minor, in Girl aet. 7½ Years Who Was Told to Sit Still; Involuntary Movements of the Face and Neck Muscles, the Right Arm and Right Leg. (After J. Ibrahim, "Lehrb. d. Kinderheilkunde," published by G. Fischer, Jena.)

Usually there is no motor paralysis; in certain cases a paresis or pseudoparesis appears, the patient behaving as though paralyzed (*chorea mollis or chorea paralytica*). The sensation and the reflexes are usually unchanged. There may be outspoken hypotony of the voluntary muscles. The eye-grounds are normal. The severer cases are usually febrile; chorea may be present when the heart is not involved (Thayer).

Among the complications the most important are (1) tonsillitis; (2) endocarditis; (3) polyarthritis, and (4) psychoses.

The *prognosis* is usually favorable; after a course of two or three months the patient recovers, though, in rare cases, the disease may last a year or more. A few terminate fatally (mortality in children 3 to 5 per cent) after great excitation, insomnia and trauma. In the fatal cases, minute disseminated foci of encephalitis are found (Poynton and Holmes, Reichardt), it is believed that the localization of these in the basal ganglia and centrum semi-ovale may stand in direct relation to the chorea (Jacob-

sohn). About 25 per cent of the cases of chorea gravidarum die. Even after apparent recovery, recurrence is not uncommon.

**Differential Diagnosis.**—(1) From choreiform movements of *cerebral palsy* (*q. v.*); (2) from *general tic* disease; (3) from *hysteria* (the so-called chorea major or magna is hysterical); in most female patients over 16 choreiform movements are hysterical (chorea hysterica); (4) from *Huntington's chorea* (age, etiology, heredity, chronicity, dementia); (5) from double athetosis (*q. v.*).

The so-called *chorea electrica* of Henoch is identical with myoclonia. Other forms of chorea electrica are probably related to the general tic disease, or to hysteria, though there may be a special infectious form separable from these.

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[Note.—See also references under Disturbances of Motility, Part XII, Sect. i.]

## 11. Chronic Hereditary Chorea

*(Huntington's Chorea, Chorea hereditaria, Chorea chronica progressiva)*

This chronic disease may occur in the same family for generations, affecting the two sexes equally. It appears, as a rule, first in middle

life, and causes choreiform movements resembling those of Sydenham's chorea. The malady is accompanied by progressive mental deterioration, which leads, ultimately, to outspoken apathy and pitiable dementia. Diffuse microscopic changes in the brain are found at autopsy (glial proliferation, disappearance of tangential fibers, etc.).

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## 12. Paralysis agitans

*(Parkinson's Disease, Shaking Palsy)*

The cause of this disease is unknown. It is common in advanced life, but is rarely encountered before forty; I have, however, seen several cases in young people. J. R. Hunt finds lesions in the globus pallidus.

**Symptoms.**—The disease is characterized by:

1. A peculiar *rigidity* of the general musculature of the body, associated with a characteristic attitude of the head, trunk and limbs.

2. A *slow tremor* (4 to 5 oscillations to the second), affecting especially the hands (pill-rolling movement of thumb and fore-finger), though extending also to other parts of the body, and occasionally to the head.

3. Slowness and difficulty of voluntary movement, with decided disinclination thereto.

4. The finer movements of buttoning and unbuttoning, of piano-playing, etc., are early disturbed. Patients complain that they cannot turn over easily in bed. A peculiar gait, with tendency, when once started, to run forward (*propulsion*) or backward (*retropulsion*). The tendency to acceleration on walking is also spoken of as *festination*

5. A tendency to diminish the size of the letters in writing (*micrographia*).

The attitudes assumed are so characteristic that, once seen, they can scarcely be forgotten; the head and trunk are bent somewhat forward, the

arms are adducted and somewhat flexed, and the legs are slighely bent at the knees. The face has a rigid, masklike appearance (*Parkinsonian mask*). Atypical cases occur; the rigidity is much more important for diagnosis than the tremor. Unilateral involvement is not uncommon at the beginning. The patients are often depressed complaining bitterly of their disability.

**Differential Diagnosis.**—In my experience, this disease, especially in its early stages and in the cases without tremor, very frequently goes unrecognized by the general practitioner. We have to differentiate it: (1) From simple *tremor senilis* (head chiefly affected; tremor not lessened on active movement; absence of characteristic rigidity); (2) from *hysteria* with which it may be combined (stigmata, coarser oscillations); (3) from *traumatic neuroses* (sensory disturbances, exaggerated reflexes, contracted visual fields, age); (4) from *multiple sclerosis* (youth, intention tremor, nystagmus, loss of abdominal reflexes, optic atrophy); (5) from *dementia paralytica* (absence of characteristic attitude, specific psychic anomalies, somatic signs); and (6) from Graves' disease, with which it may be combined (tachycardia, struma; finer, more rapid, tremor; eye-signs).

Fig. 624.—Severe Form of Paralysis agitans with Typical Attitude and Characteristic Facial Expression—Twenty Years After Onset. (After H. Curschmann, "Lehrb. d. Nervenkr.," published by J. Springer, Berlin.)

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## 13. Myasthenia gravis pseudoparalytica

*(Bulbar Paralysis without Anatomical Findings, Asthenic Bulbar Paralysis, Myasthenic Paralysis, Myasthenia gravis pseudoparalytica, Erb-Goldflam Symptom-Complex)*

**Definition.**—A condition characterized by a quick fatigability of the muscles (*myasthenia*), manifesting itself in difficulty in chewing (*dysmasesia*), in speaking (*dysarthria*), and in swallowing (*dysphagia*). Besides the paresis in the domain of the bulbar nerves, myasthenic symptoms are noticeable elsewhere in the body (M. levator palpebrae; muscles of the trunk and extremities; respiratory muscles). There is no muscular atrophy, and no DeR. There is a marked tendency to remissions and exacerbations. Disturbances of sensibility are absent, but on electrical examination a characteristic myasthenic reaction (*q. v.*) appears.

In double ptosis, with diplegia facialis, the face has a peculiar characteristic appearance. Owing to the weakness of the M. orbicularis palpebrarum, the patients are unable firmly to close the eyes (lagophthalmus). At autopsy no neural lesions have been made out, though small mononuclear cell infiltrations have been found in the muscles (Weigert, Buzzard), and in other organs. Some investigators regard the disease as of muscular origin rather than of nervous origin. In a patient that I saw with Dr. I. J. Spear, lymphocytic foci were demonstrable in a piece of muscle excised for diagnosis.

Many of the patients have shown a persistent thymus. It may be that the disease is due to a disturbance of the endocrine glands. Some authors have already called attention to the myasthenia that often complicates

Graves' disease, and which has been thought to be due to adrenal insufficiency. Others have referred the affection to a hyperfunction of the parathyroid glands (the opposite of tetany).

The patients go through periods during which there is a remarkable remission of the symptoms, so that they, and often their physicians, think that they are cured. I know of one and the same case that has been reported as "cured myasthenia gravis" at medical societies on several different occasions. The prognosis is, in reality, grave; death occurs in at least two-thirds of the cases after a shorter or longer course.

Fig. 625.—Myasthenia gravis. (Med. Service, J. H. H.)

**Differential Diagnosis.**—It is very important not to mistake the nature of the disorder. Many consultants have "slipped up" before becoming familiar with this disease. It must be differentiated (1) from *hysteria* (bulbar symptoms not so characteristic; fatigability not demonstrable; myasthenic reaction absent); (2) from *true bulbar paralysis* (progressive course, atrophy of the muscles, DeR); (3) from *poliencephalomyelitis* (atrophy of muscles, depression of electrical excitability, progressive course, no recovery of the muscles on rest); (4) from *primary myopathies* (pseudohypertrophy or atrophy of the muscles, electrical examination).

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## 14. Periodic Family Paralysis

**Definition.**—A periodic paralysis affecting members of certain families, the single attacks coming on especially after a long rest, after sleep, or after overexertion. The attacks last, as a rule, several hours; they may continue only fifteen minutes or they may persist as long as a week. Some patients have attacks once a day or once a week; others only at intervals of a month, several months, or several years. The mechanical excitability of the muscles is diminished. The toxicity of the urine is increased.

The condition has been studied in this country by Mitchell, Flexner, and Edsall. Dr. Holtzapple, of York, Pa., has had under his observation a family in which several members suffer from this malady. The nature of the disease is unknown, though obscure metabolic disturbances are probably responsible.

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## 15. Periodic Oculomotor Paralysis

**Definition.**—A condition in which oculomotor paralysis sets in periodically (usually at regular intervals), and lasts for a few days or weeks, and then disappears completely, or almost completely. Children are more

often affected than adults, and do not necessarily come from notably neuropathic ancestors. The affection is unilateral, involving always the same eye, and is associated with headache on the side of the paralysis, or with pain in the eye on that side, and with nausea and vomiting, thus suggesting a kind of migraine attack. Usually the headache ushers in the attack; it ceases when the paralysis appears. The headache and the vomiting may, however, last for a week.

The paralysis of the N. oculomotorius is usually total; sometimes only the external muscles of the eye are involved, or a single muscle only (M. levator) may be paralyzed.

The nature of the disease is unknown, and may not be unitary. Oppenheim regards it as related to migraine, and thinks that it is due to vasomotor disturbances.

## 16. Myotonia congenita

(*Thomsen's Disease*)

**Definition.**—A familiar, and also an hereditary, disease, characterized by (1) enlargement of the muscles, and (2) interference with the voluntary movements due to a rigidity that sets in on attempting to make them. Thomsen, who described it, was a member of a family in which the disease prevailed, twenty cases having been observed during four generations.

The enlargement of the muscles is usually a striking feature. I remember a child, shown by Dr. W. B. Platt at a medical society, in whom the muscles were exceedingly hypervoluminous, like those of an adult athlete.

Sudden movements, requiring the exertion of considerable force, are the ones most disturbed. The patient cannot open or close his fist rapidly; he cannot turn suddenly when walking. A kind of hypertonus sets in in the muscles, and this cannot be inhibited by the will.

Usually the whole body is affected; sometimes certain muscles only. Even the eye-muscles may be involved. Excitement exaggerates the difficulty of movement, as does also exposure to cold.

The mechanical excitability of the muscles is increased, that of the nerves diminished. On electrical examination the so-called myotonic reaction appears (*q. v.*). Despite the hypertonus of the muscles, the knee-jerks are diminished, or absent.

The disease has often been associated with other nervous diseases (epilepsy, migraine), occasionally with one of the myopathies. Some authors regard the combination of myotonia with muscular atrophy as a special form of myopathic dystrophy (Steinert, Batten and Gibb); such an atrophic myotonia begins late (20-30), is limited to a few muscles (hand, forearm, sternocleidomastoid, and facial muscles), and is often

associated with general emaciation, atrophy of the testicle, loss of knee-kicks, cataract, and speech disturbances.

Closely related to Thomsen's disease is the so-called *paramyotonia congenita* (Eulenburg), in which the rigidity comes on only during exposure to cold; it is followed by a paresis, which lasts for several days. In this form the mechanical excitability of the muscles is not increased, and there is diminished excitability on electrical examination.

Many atypical forms of Thomsen's disease are reported in the bibliography (Pelz, Oppenheim).

Thomsen's disease does not shorten life, but it is not amenable to treatment. Excised particles of muscle show a hypertrophy of the primitive fibers and an increase in the sarcolemma nuclei.

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## 17. Amyotonia congenita

(*Myatonia congenita, Oppenheim's Disease*)

**Definition.**—A congenital affection, characterized by a peculiar symmetrical paralysis, especially of the musculature of the lower extremities, associated with marked atony of the muscles, the condition resembling,

superficially, the infantile paralysis of poliomyelitis (Oppenheim, 1900). The extremities hang loose and flop about, owing to the atony. The knee-kicks and ankle-jerks are usually absent. There is no visible atrophy of the muscles. Electrical excitability is depressed or abolished. The children seem to be paralyzed, though some movements can be performed.

The condition has been carefully studied in England by Collier, Holmes and Wilson, and in this country by Spiller and Griffith.

**Etiology.**—The cause is unknown. The disease is not familial in char-

Fig. 626.—Myatonia (amyotonia) congenita. (After Collier and Wilsosn in "Brain," published by Macmillan & Co., New York.)

acter. The mothers of the children have often stated that they felt no "quickening" when carrying the child.

Autopsies have revealed some atrophy of the muscles and a diminution in the number of the anterior-horn cells.

Some authors have tried to identify the disease with the Werdnig-Hoffmann type of progressive (central) muscular atrophy, others to make it a form of fetal poliomyelitis.

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Fig. 627.—Dystonia musculorum deformans. (After H. Oppenheim.)

## 18. Dystonia deformans progressiva

(*Dysbasia lordotica progressiva of Oppenheim, Tonic Torsion Neurosis of Ziehen, Progressive Torsion Spasm in Children of Flatau-Sterling, The Ziehen-Oppenheim Disease*)

**Definition.**—A chronic, progressive, disease, appearing usually in children between the ages of 8 and 14, and characterized by a twisting of the whole body, especially of the trunk, on standing and on walking. During movement there is marked lordosis, with some skoliosis, and twisting of the pelvis (*tortipelvis*), due to the muscular cramps; these deformities disappear, almost wholly, when the patient is at rest. In the recumbent position all signs of motor irritation disappear, or nearly disappear; the symptoms come out only on attempts at voluntary movement, thus differing markedly from what we see in double athetosis. Certain muscles show a continuous hypertony, others a continuous hypotony.

The grotesque attitudes, especially on walking, have suggested the designation "dromedary gait" or "camel's walk."

The disease is most common in the children of Russian Jews. I have

seen it once in an American physician. He had suffered in earlier life from spastic torticollis.


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## K. The Angioneuroses and the Trophoneuroses

Aside from those that are especially symptomatic of other diseases we may consider:

(1) Acroparesthesia; (2) angioneurotic edema; (3) Raynaud's disease; (4) erythromelalgia; (5) hydrops articulorum intermittens; (6) progressive facial hemi-atrophy; and (7) scleroderma.

### 1. Acroparesthesia

(*Vasomotor Neurosis of the Extremities of Nothnagel*)

Common in women in middle life (menopause). Cause unknown. The symptoms are subjective (paresthesias in the hands and fingers, especially at the tips; pains), worse at night and in the early morning, interfering with the finer kinds of work; slight hypesthesia sometimes demonstrable. It usually lasts for years.

It is probably due to an irritative state of the vasomotor centers, causing vasoconstriction of the acra.

**Differential Diagnosis.**—We must keep in mind the possibility of (1) *gliosis spinalis;* (2) *Raynaud's disease;* (3) *tabes;* (4) *beginning acromegaly;* (5) beginning *ataxic paraplegia* in pernicious anemia; and (6) *chronic tetany.*

### 2. Angioneurotic Edema

(*Acute Circumscribed Cutaneous Edema, Hydrops hypostrophos, Quincke's Disease*)

**Definition.**—A paroxysmal, circumscribed edematous swelling of the skin, subcutaneous tissue or mucous membranes, appearing suddenly,

localized either in a single area, or simultaneously involving different areas over the body, and lasting from a few hours to a day or two. The eye-lids, lips and cheeks are most often affected. Occasionally the gastric or intestinal mucous membrane (abdominal crises), the glottis (often with fatal termination), or the joints are involved.

Fig. 628.—Acute Circumscribed Angioneurotic Edema of Quincke. (From v. Zumbusch's Article in Riecke's "Lehrb. d. Haut u. Geschlechtskr., published by G. Fischer, Jena.)

Certain cases of meningitis serosa may belong here. It is also possible that a local cerebral edema resembling an apoplectic insult may occur in this disease. The writer has observed cases that he believed to be of this nature.

The cause is unknown, though the condition is met with chiefly in psychoneurotic persons; a peculiarity is that males are more often affected than females. Certain families are especially prone to attacks. I know a physician whose wife suffers from the disease; he keeps a tracheotomy outfit always at hand, several members of his wife's family having died of edema glottidis.

## 3. Symmetrical Gangrene

(*Raynaud's Disease, Symmetrical Local Asphyxia*)

In symmetrical areas of the skin, usually the ends of the fingers or toes, there occurs paroxysmal paresthesia with marked anemia (*local syncope,* "dead fingers"), followed later by cyanotic discoloration (*local asphyxia*). The circulation may return to normal, but in some cases partial necroses, and, in rare instances, total necrosis, of a whole digit may result (*local gangrene*).

Occasionally other acra (tip of nose, ear lobules) may be involved.

There is no fever. The pain may be severe. Insomnia, gastric disturbances, and depression are common accompaniments of an attack.

The pathology is obscure (central disease of vasomotor paths and centers?). Monro, of Glasgow, has made a careful clinical study of the condition. Patients usually remain free from attacks if they go far enough South in winter.

**Differential Diagnosis.**—(1) From *arteriosclerotic gangrene;* (2) from *diabetic gangrene;* (3) from *gliosis spinalis* (syringomyelia, Mor-

Fig. 629.—Symmetrical Gangrene in Raynaud's Disease. (After Dehio, Deutsche Ztschr. f. Nervenheilkunde.)

van's syndrome); (4) from *acrocyanosis chronica anesthetica* (gradual development, absence of paroxysms); (5) from *lepra mutilans* (painless); and (6) from *thrombo-angiitis obliterans* (fever; Jewish race).

## 4. Erythromelalgia

*(Weir Mitchell's Disease)*

This rather rare condition is characterized by pains in, and redness of, the skin in the distal portions of the lower or upper extremities, or both; it is sometimes associated with headache, vertigo, tachycardia and syncopal attacks, occasionally with polycythemia (Osler).

## 5. Hydrops articulorum intermittens

*(Hydrops hypostrophos)*

**Definition.**—A rare condition with sudden, periodically recurring, serous exudation into a joint (most often the knee), on one or both sides, without redness, and usually without fever, lasting from one day to a

week. The swelling may be complicated by, or alternate with, cutaneous hemorrhages, pains in the extremities, or asthmatic attacks. The condition usually persists for years.

## 6. Progressive Facial Hemi-atrophy

(*Hemiatrophia facialis progressiva*)

**Definition.**—A rare condition appearing in adolescence, without apparent cause, and characterized by a gradual atrophy of one-half of the face, setting in usually at one, or more, special points (cheek, orbit, lower jaw). All the tissues (bones, muscles, connective tissue, skin) are involved.

The pathogenesis is obscure (autonomic nervous system?). Progressive facial hemihypertrophy has also been met with.

## 7. Scleroderma

**Definition.**—A condition in which the skin is hardened, shrunken and atrophied; it is firm to the feel and cannot be lifted from the subjacent parts; pigmentary changes and vasomotor changes (pallor, cyanosis, mottling) are common accompaniments. Whether scleroderma is a primary

Fig. 630.—Scleroderma of Both Hands and Forearms. From the Leipzig Medical Clinic. (After Tomasczewski in Riecke's "Lehr. d. Haut u. Geschlechtskrankh.," published by G. Fischer, Jena.)

disease of the skin, or of the sclerotomes, or is a trophoneurosis, is not known.

The disease may occur at any age. Females are much more often affected than males.

Sometimes local areas of the skin only are involved; in other cases the process extends to a large part of the body. Among the sites of predilection may be mentioned the skin of the face, of the neck and of the upper half of the trunk, and of the upper extremities, especially the hands. The lower extremities are less often involved. The disease may be unilateral, but is more often bilateral.

A segmental topography has been emphasized. On account of the involvement of the connective tissue and of the bones in many cases, I have thought that we might, here, be dealing with a primary disease of the sclerotomes.

At the beginning the skin may appear edematous and hypertrophic. This early stage soon gives way, however, to induration, the skin becoming hard, tense, and glossy. Finally, the atrophy becomes marked. When the hands have become stiff and crippled from the disease, and the bones thinned, the condition is known as *sclerodactyly*. Sometimes a single finger may undergo ringlike constriction, as in *ainhum*.

The patients who suffer from this disease usually show marked signs of deprcciation of the general health. The outlook is bad, the disease being usually progressive. I have often observed an associated thyreopathy.

**Differential Diagnosis.**—We must distinguish the disease (1) from *progressive facial hemi-atrophy;* (2) from *dermatomyositis;* (3) from *Dupuytren's contracture;* (4) from *Raynaud's disease;* and (5) from the atrophic and distorted hands of *chronic progressive polyarthritis.*

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## L. The Psychoses or Insanities

Though mental diseases belong to the domain of a special branch (psychiatry), they are met with, especially in their early stages, by every practising physician, and very serious errors often result from the poor training that medical students have thus far received in the recognition and treatment of abnormal mental states. For this reason it seems desirable to pay some attention to the diagnosis of the commoner forms of insanity in a textbook dealing with general medical diagnosis. For details the reader must consult textbooks of psychiatry.

Most people who go insane are the victims of bad heredity (psychopathic predisposition), many of them showing stigmata of degeneration (*q. v.*). They are unable to bear the strain of the struggle of existence,

or of infection and intoxication. Certain periods in life (puberty and the period of involution), as well as certain physiological processes (pregnancy, lactation), are times of especial danger. Chronic alcoholism, drug habits and infectious diseases, especially syphilis, and certain disorders of metabolism (gout, nephritis, auto-intoxications) are sometimes of influence. Psychic shocks are also of importance. Brains born normal may become so diseased that insanity ensues (this is notably so in many cases of dementia paralytica, atherosclerosis, infectious psychoses, and psychoses complicating tumor cerebri).

It is customary to separate the mental diseases due to coarser organic change from the so-called functional insanities, but there can be but little doubt that the latter depend upon structural alterations too fine for recognition by our present methods.

We shall consider the diagnosis of the following:

1. The manic-depressive group of psychoses.
2. The paranoid states.
3. The dementia precox group.
4. The infectious, toxic and exhaustion psychoses.
5. The alcoholic psychoses.
6. Psychoses related to drug habits.

The mental disturbances depending upon other forms of organic disease (dementia paralytica; cerebral atherosclerosis and senile dementia; lues; tumor cerebri; multiple sclerosis) have been referred to already, in connection with the diseases underlying them. The hysterical and epileptic insanities have also been mentioned under the psychoneuroses.

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[NOTE.—For other references, see Psychiatric Methods of Examination, Part XII, Section i.]

## 1. The Manic-Depressive Group of Psychoses

There is a group of psychoses characterized by manic states (*manias*), by depressive states (*melancholias*), or by mixed manic-depressive states. In some cases the patients suffer from only one attack, either of mania or of melancholia; not infrequently there is a regular recurrence (cycle) of the two opposite states of mania and melancholia, the single cycles repeating themselves, after shorter or longer free intervals, throughout the whole life-time (*circular insanity,* or *cyclothymia*).

### (*a*) *The Manic Phase* (*Mania*)

In the "manic phase," or maniacal state of this psychosis, the patients experience and manifest an exalted mood; they tend to sudden changes in humor, to flight of ideas, to easy distraction of the attention, and to so-called "pressure of activity" in occupation. In the exaltation, everything is easy for the patient, and he sees the world in a rosy light. The facial expression is happy, though subject to rapid change to anger. There are rapid changes in the direction of the ideas; the patient seems unable to hold a "goal idea" in mind, objects about him quickly altering the flow (superficial associations). There is a tendency to make rhymes, puns, and alliterations. The "pressure of activity" exhibits itself as a preternatural loquacity, or in a tendency to excessive business, in the writing of many letters, in the sending of many telegrams, in the making of unnecessary purchases, in unnecessary travelling, visiting, etc. Such patients are also prone to indulge in sexual and alcoholic excesses.

Mild forms (*hypomania*) sometimes go unrecognized; indeed the pa-

tients are often thought to be unusually healthy and vigorous (blooming appearance, bright eyes, sharp observation, rapid conversation). The trained physician, however, quickly recognizes the superficiality of it all, the poverty of the underlying thought, the tendency of the mental associations to be influenced by sound, similarity, and contiguity, the resemblance to mild alcoholic intoxication, and the absence of disease insight.

In the severer forms of mania there may be delusions of grandeur and of extravagant self-appreciation; there may also be hallucinations, though these are not common. The mood changes suddenly; without warning there may be an increase of irritability or an outbreak of anger and violence. The patients may "break loose," attack their surroundings, and explode into blackguardism (*mania furiosa*). They gesticulate, dance, yell, tear up their clothes or pull out their hair. In the wilder cases sexual acts may be publicly performed or the patients may smear themselves with urine or feces. Under all this maniacal excitement the patients may experience no feeling of fatigue.

In milder cases the orientation may be good, but in the severer forms, especially those with many hallucinations, there is disorientation and confusion (maniacal confusion).

The patients lose weight rapidly from insomnia, lack of food and excessive movement. After several months, during which remissions and exacerbations occur, the patients may gradually improve, regain their weight, and return approximately to normal.

The manic states have a marked tendency to recur. The first attack usually appears in youth (15 to 25).

**Differential Diagnosis.**—A maniacal attack of the manic-depressive group must be distinguished from the maniacal attacks in (1) *dementia paralytica* (somatic signs, progressive dementia, positive Wassermann, cytodiagnosis of cerebrospinal fluid, anamnesis); (2) *catatonic states* of dementia precox (apathy, stereotyped movements, verbigeration, negativism); (3) *hallucinatory confusion,* or *amentia* (loss of comprehension, absence of exaltation).

### (*b*) *The Depressive Phase*

The depressive phase or melancholic state of the manic-depressive psychosis is characterized by a pathological sadness and a slowing of thought and of emotion, associated with micromanic delusions (ideas of self-depreciation, ideas of poverty, ideas of sin, hypochrondriacal ideas, etc.). The milder forms, in which the emotional disturbances are slight, are called simple melancholia (*melancholia simplex*); the severer forms are sometimes spoken of as anxious melancholia (*melancholia agitata*). *There is always danger of suicide.* Digestion is disturbed; the tongue is coated, the breath is fetid and the bowels are constipated. In the milder cases

the patients admit that they are sick; in the severer cases they deny that they are sick, and assert that they are sinful.

A large part of the involutional psychoses (senile, presenile, and climacteric psychoses) take the form of melancholia.

**Differential Diagnosis.**—The psychomotor retardation is the clue to diagnosis, and distinguishes depressive phases of the manic-depressive psychosis from other forms of depression. It must be differentiated from (1) depressive phases of *dementia paralytica* (real dementia, somatic signs, Wassermann reaction); (2) from depressive *catatonic states* (apathy and indifference, negativism, mannerisms, course); (3) from depressive stages of *senile dementia* (intellectual deterioration).

### (c) *Mixed Manic and Depressive States*

Not only are depressive symptoms prone to alternate with symptoms of exaltation, but states are met with in which some of the manic symptoms are combined with some of the depressive symptoms. Association tests are helpful in recognition.

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## 2. The Paranoid States

By a paranoid state is meant a form of mental disturbance in which delusion, more or less systematized in character, and, especially, delusions of persecution and of grandeur develop, with or without hallucinations.

A paranoid state may develop acutely (*paranoia acuta*), or it may develop, and grow into a system, with progressive increase in delusions (*paranoia chronica*).

The *acute paranoid states* are common in chronic alcoholism, taking especially the form of the "acute jealousy-insanity." A similar jealousy-insanity sometimes develops in the puerperium, or during lactation.

In the *chronic paranoid states,* there are anomalies both of the intellect and of the emotions. The disease develops so slowly that for many years a psychosis may not be suspected. The patient is often hypochondriacal, retiring, suspicious, and suffers from ideas of reference (*q. v.*). Later, ideas of persecution appear (people treat him badly, "have it in for him," are trying to poison him, etc.). Egocentric, grandiose ideas usually develop (ideas of unusual personality and powers, revelations from God, royal descent, ideas of reform and of discovery). In some cases hallucinations (voices, visions) are prominent (*paranoia chronica hallucinatoria*).

According to the nature of the delusions, the paranoid states are described as erotic mania, religious mania, political mania, jealousy mania, etc. Paranoiacs are often dangerous to other people.

Most cases can be placed in one of two groups: (1) true chronic paranoia, and (2) dementia paranoides (one variety of dementia precox). In the latter the course is much quicker, the delusions are more nonsensical, and a high grade of confusion and dementia may soon appear.

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## 3. The Dementia precox Group

(*The Adolescent Psychoses, the Schizophrenic Psychoses*)

By the psychoses of adolescence (dementia precox) are meant a group of mental anomalies presenting marked individual variations, but all having in common, (1) development about the time of puberty or at any

rate in the first half of life; and (2) termination, sooner or later, in a dementing process, of variable grade. Not all reach a high grade of dementia; in some cases, there is arrest with defect; in a very few cases, there may be complete recovery.

The cause is unknown, though it is probably some deep-seated vice of metabolism, causing severe and extensive injuries to the cerebral cortex.

In diagnosis, the episodic states are less important than (1) the motor symptoms, and (2) the development of a progressive dementia in youth.

Among the variable clinical pictures met with in the adolescent psychoses, three main types may be distinguished: (1) hebephrenia, (2) catatonia, and (3) dementia paranoides.

The most interesting recent monograph on dementia precox is that of Bleuler (1911). Starting out from Kraepelin's conception of dementia precox as a definite syndrome that tends to result in dementia, thus differing from acute mental diseases like the manic-depressive psychosis that never go over into dementia, Bleuler has set up a still wider conception, known as *schizophrenia,* which includes what has hitherto been known as dementia precox and also a series of other states not hitherto classed with it. Bleuler uses the term "schizophrenia" because he believes that the cleavage of the different psychic functions is the most important characteristic of the group of conditions under consideration. He recognizes, however, that schizophrenia includes several undoubtedly different diseases. The mental states thus designated run sometimes a chronic course, sometimes an intermittent course; the disease may be arrested at any stage, or it may recede, but there is probably never complete recovery. The mental state is specific, leading to an alteration of thought, of feeling, and of relations to the external world, not met with under other conditions.

"The cleavage of the psychic functions is more or less distinct in every case. When the disease is advanced, the unity of the personality is lost, the person being represented sometimes by this, sometimes by that, psychic complex. The reciprocal influence of the different complexes and strivings is insufficient or absent. The psychic complexes no longer flow together as in health to form a conglomerate of strivings with unitary resultants, but one complex dominates at times the personality, other groups of ideas and strivings being split off and becoming wholly, or at least partly, ineffective. The ideas of the patient are incomplete, fragments of ideas becoming incorrectly fused to form new ideas. Thus the patient's conceptions lose completeness since they are deprived of one or of several, often essential, components; indeed, in many cases, the conceptions are represented only by single parts of ideas."

Bleuler points out that the associative activity is also often determined by fragments only of ideas and conceptions; on this account, besides mistakes, there is something bizarre about the associations, something one would never expect to meet with in a healthy person. Thus, the associative activity may stop suddenly in the middle of a thought, or when it should proceed from one to another thought; instead of continuing in a normal way, new ideas that neither the patient nor his auditor can connect with the earlier content of thought may suddenly arise.

On the other hand, primary disturbances of perception, of orientation, and of memory are not demonstrable. The affective life is, however, markedly disturbed. In the severest cases, no expressions of feeling can be observed. In the milder cases, it is noticeable that the degree of the feeling-reactions to experiences do not stand in correct relations to one another; the intensity of feeling can oscillate

between complete absence of expression of feeling and an exaggerated affective reaction. Moreover, the affective states may appear to be qualitatively abnormal, inadequate to the accompanying intellectual processes.

In addition to the signs of dementia, the majority of advanced cases of schizophrenia show still other symptoms, including hallucinations, delusions, confusional states, twilight states, manic and melancholic affective states, twilight states, manic and melancholic affective states and catatonic symptoms. Bleuler emphasizes that in these *accessory symptoms and syndromes* a specific schizophrenic character can often be made out, and that they also, when they are present, can be used for purposes of diagnosis. In milder cases, not under treatment in institutions, schizophrenic states are often met with in which the accessory syndromes are absent, or present only to a slight degree.

Bleuler divides schizophrenia or dementia precox into four subdivisions:

(1) *The Paranoid.* Hallucinations or delusions or both stand permanently in the foreground.

(2) *The Catatonic.* Catatonic symptoms stand permanently, or at any rate for a long time, in the foreground.

(3) *The Hebephrenic.* Accessory symptoms occur without continuously dominating the picture.

(4) *The Simple Schizophrenic.* During the whole course only the specific fundamental symptoms are demonstrable.

In describing the symptoms, Bleuler emphasizes the importance of knowing that these are all transitions from the normal, and that the mildest cases, or so-called *latent* schizophrenias, with symptoms scarcely recognizable, are much more numerous than the *manifest* cases. Moreover, owing to the great variations in the schizophrenic syndrome, one must not expect to be able to demonstrate every symptom at any one time.

Bleuler divides the symptoms into, (1) fundamental symptoms, and (2) accessory symptoms.

The **fundamental symptoms** are formed by the schizophrenic disturbance of association and affectivity, by a tendency to place the personal fantasy above reality and to exclude the latter (autismus). In addition, as fundamental phenomena, Bleuler includes the absence of symptoms that play an important rôle in certain other diseases (*e. g.,* primary disturbances of perception, of orientation, of memory, etc.).

Thus, the *altered simple functions* include (1) loosening of the associations and sudden arrests of associative activity, (2) a change in the feelings to apathy and indifference, and (3) the tendency to ambivalence. By "ambivalence" is meant the giving of both a negative and a positive response, simultaneously, to different psychisms; for example, a certain idea may be simultaneously accompanied by pleasant and by unpleasant feelings ("affectivity-ambivalence"), as when a husband both loves and hates his wife. In "ambivalence of will," the patient may try to eat and not to eat at the same time, bringing the spoon many times to the mouth without taking the food. In "intellectual ambivalence," the patient may say in one breath that he is Dr. A. and that he is not Dr. A. There is every transition from ambivalence to outspoken negativism.

Among the *"intact" simple functions,* Bleuler includes sensation and perception, orientation, memory, awareness and motility.

Among the fundamental symptoms Bleuler includes the following *alterations of the more complex functions:*

(1) The relation to reality, these patients manifesting autismus; (2) the attention; (3) the will; (4) the person; (5) the intelligence and (6) the behavior.

In "autismus," the patients live in a world by themselves, limiting their contact with the external world as much as possible. This cutting loose from reality, together with the relative and absolute predominance of the internal life, is what Bleuler calls autismus. It is almost synonymous with Freud's "autoerotismus" and with P. Janet's "loss of the sense of reality."

As regards the "attention," it suffers also as a fundamental symptom. While it may seem normal for any interests that remain, still, owing to the absence of affective states, there is a lack of the impulse to follow external and internal processes and to direct the senses and the thoughts; in other words, there is an enfeeblement of the active attention. The passive attention is altered in a different way; though no interest may be manifested in what goes on about the patient, he may, nevertheless, register in a remarkable way nearly everything that goes on about him.

The "will," which is the resultant of all the different affective and associative processes, is fundamentally disturbed, this disturbance being manifest, especially in the depression of the feelings. In milder cases, the aboulia of the patients may bring them into conflict with their surroundings. They grow lazy and negligent, having no longer any impulse to do anything either from personal initiative or on command. They may lie for years in bed, or, if up and about, do nothing to favor the realization of their wishes. On the other hand, such patients may sometimes present a hyperboulia, when they will carry through with great energy anything that they undertake, be it reasonable or nonsensical, without regard to those about them. A combination of feeble will with obstinacy is by no means uncommon.

As regards the "person," these patients are autopsychically oriented. They know who they are; but the ego is, nevertheless, not wholly intact; it shows a tendency to cleavage.

On the "intellectual side," the dementia in schizophrenics is best seen on examination of their associations and of their affectivity. There is no actual loss of memory, so that some authors speak of "pseudodementia" rather than of "dementia;" the condition thus differs fundamentally from what one sees in the so-called organic psychoses that lead to dementia or from what one sees in idiocy in which only relatively few memories are acquired. In the severe schizophrenic states, besides the marked lack of interest and of activity, one may observe many faults in the thought-processes and in the performance of acts; whether the task set is difficult or easy is of subordinate importance. In the mildest forms, though the patients are ordinarily entirely reasonable, they are quite capable in certain circumstances of performing almost any foolish action. Thus, a patient, who at one time cannot add 17 and 14 even when he tries seriously to do so, may solve immediately a difficult calculation or give an orderly and successful speech; or a patient, who for years has sat in a demented, though euphoric state, upon a bench, and has given expression to nothing but the most banal phrases, may, all at once, participate in all kinds of work and seem, at home, to be in every way cured. As Bleuler puts it, the schizophrenic is not demented in the simple sense, but is demented in regard to certain times, certain constellations, certain complexes.

As regards the "behavior" of the patient, the outspoken schizophrenic shows loss of interest, lack of initiative, and absence of a definite goal, through insufficient adaptation to the surroundings, that is, by leaving unconsidered many factors of reality on account of distraction through sudden ideas and eccentricities.

The milder (latent) cases live essentially like other people and are thought to be well; at most, they attract attention through hypersensitiveness and, here and there, through a bizarre action. They may be active in simple occupations or even sometimes in an artistic or an academic way. The most striking things about the

milder cases are their irritability and sensitiveness to little things, their unpleasant stubbornness, and their moodiness.

Among the **accessory symptoms** of schizophrenia Bleuler includes, (1) hallucinations, (2) delusions, (3) accessory disturbances of memory, (4) alterations of personality, (5) alterations of speech and writing, (6) certain bodily symptoms, (7) catatonic symptoms (catalepsy, stupor, hyperkinesis, stereotypy, mannerisms, negativism, command-automatism and echopraxia, automatism, impulsive acts), (8) various acute syndromes (melancholic states, manic states, catatonic states, delusional insanity, twilight states, mental dullness, confusion and incoherence, outbreaks of anger, excitement on certain definite days, stupor, deliria, *fugues* and dipsomania.)

The distinction between primary and secondary symptoms is essential to Bleuler's conception of the disease. He believes that the disease is a process that directly causes the primary symptoms, whereas the secondary symptoms are partly psychic functions under altered conditions, partly the results of more or less unsuccessful, or even of successful, attempts of adaptation to the primary disturbances.

Bleuler discusses the question whether or not a physical disease process need be absolutely necessarily presupposed in schizophrenia. Some believe that the whole symptomatology is psychically conditioned and that it can develop on slight deviations from the normal, very much as the tendency to hysterical symptoms is so great in many people that in the ordinary difficulties of life they become hysterical, whereas the average person becomes hysterical only after extraordinary psychic traumata. Though certain pathological-anatomical findings have been demonstrated, these are attributed by Schott to inactivity-atrophy or by Young to the results of toxins formed during the emotional states. The symptoms are fundamentally different from those of all known organic or toxic disturbances, and are so much like those of the so-called functional neuroses that mild schizophrenic cases are often supposed, for a long time, to be hysterical or neurasthenic. Bleuler values, however, the arguments against schizophrenia being a purely functional process and points out, especially, that the incurability and the insusceptibility to influences as regards the course of most cases are without analogy in purely functional disturbances. Moreover, the disease occurs among savages as well as among cultured peoples. It may be, therefore, that an anatomical or chemical disturbance, which runs a chronic course with acute exacerbations and periods of arrest, causes the primary symptoms (loosening of associations; disposition to hallucinations, to stereotypy, etc.); but just what the nature of the schizophrenic process is, no one as yet knows.

### (*a*) *Hebephrenia*

The picture may be that of a simple progressive dementia, or of a dementia complicated by episodic states of depression, excitation, or delusion.

A youth of promise, at puberty, or soon after, begins to stand still or to retrograde mentally; parents and teachers attribute this to laziness, to distraction, or to bodily disorders (onanism, menstrual disturbances).

The patients are often treated, at first, as neurasthenics. They tend to change their occupation frequently, have an exaggerated idea of their own importance, tend to occupy themselves with the deepest problems of existence, show pleasure in resounding phrases and dry proverbs, or abnor-

mally devote themselves to puns and to practical jokes. Signs of feeble judgment soon appear. They write long theoretical treatises, publish impossible books or undertake impractical careers. Among the complicating episodic states may be mentioned sudden depression, excitation, anxiety, or suicidal tendency. Each episodic state is followed by deterioration and by increase of apathy.

**Differential Diagnosis.**—The cases usually go unrecognized for some time, and are designated *neurasthenia,* or *hypochondriasis.* The physician should always be suspicious of hebephrenia in young people with good memory and comprehension who exhibit loss of initiative, dulling of the higher feelings, or a sense of failure of intelligence, particularly when no special cause for exhaustion is demonstrable and when the symptoms are not easily gotten rid of by general hygienic measures.

### (*b*) *Catatonia*

One of the commonest forms of insanity in young people is that characterized by (1) specific catatonic phenomena (negativism, command-automatism, stereotypy, grimacing, anomalies of speech and writing), (2) episodic states of stupor or excitation, and (3) a termination (generally) in dementia.

After a brief period of mental depression at the onset, the patients suddenly begin to behave in a surprising manner. Without apparent cause they may suddenly refuse to take food, or they may remain away from home without cause, or they may enter upon some "impossible" marriage-engagement. Sooner or later, symptoms of catatonic excitation develop. In a few cases, the patients commit suicide early in the disease, the family not having suspected the existence of a psychosis.

In *catatonic stupor,* there is a peculiar alteration of psychomotor innervation, including negativism, in which the patient shows resistance (1) to any external influence on his will, and, also, (2) to spontaneous motor impulses arising in himself (refusal to speak, to show the tongue, to take food, to swallow saliva). Muscles once innervated may retain their innervation, giving rise to the so-called "stereotyped attitudes" (inclined head, crossed legs, snoutlike projection of mouth, turned-in thumbs, etc.). These attitudes may be maintained for hours, days, or weeks, despite discomfort or ulceration from pressure.

In *command-automatism,* on the other hand, there is, in contrast with negativism, a preternatural suggestibility in the motor domain, exhibited as waxy flexibility (*q. v.*), echolalia, and echopraxia.

In *catatonic excitation,* violent, purposeless movements are made, often with loud cries and attacks upon surrounding people; sometimes there are suicidal attempts. The so-called "monotonous, or stereotyped, movements" (rhythmical swaying of body, rubbing of hands, movements of tongue,

etc.), kept up for hours, or days, at a time, represent a transition stage between catatonic stupor and catatonic excitation.

In intervals between excitation and stupor, certain peculiarities of behavior usually remain (grimacing, motiveless laughing or crying, aërophagia, peculiar writing, tendency to verbigeration, irrelevance, mannerisms). On the psychic side, there is (1) a slow enfeeblement of the judgment, though the recording faculty and the memory may be good, (2) a dulling of feeling and apathy, (3) sometimes delusions, and (4) an incalculability and bizarreness of behavior.

Certain *somatic signs* may coexist (exaggerated reflexes, heightened mechanical excitability of muscles and nerves, increased secretion of sweat, sebum and saliva; amenorrhea, subnormal temperature, pupillary anomalies (Bumke), remarkable variations in body weight, occasionally epileptoid signs). Remissions and exacerbations are common.

**Diagnosis.**—The catatonic phenomena, alone, do not suffice for the diagnosis of dementia precox, for they are met with, temporarily, in other psychoses. The combination with mental enfeeblement is essential. The differentiation from *dementia paralytica* (lumbar puncture), *epilepsy, hysterical twilight states,* or *amentia* (disturbance of comprehension, disorientation, etiology) is usually easy. In *imbecility* and *idiocy* the patients have been intellectually feeble from early childhood, whereas in dementia precox there is a demonstrable deterioration of the mental powers. The differentiation from a *manic-depressive psychosis* is not always easy, but the apathy, the negativism, and the evidences of actual mental deterioration will usually be decisive.

### (*c*) *Dementia paranoides*

This form of adolescent psychosis (less common than hebephrenia, or catatonia) is characterized by a rapidly advancing delusional state, in which the delusions quickly become most surprising and nonsensical, terminating relatively quickly, or in a few years, in feeble-mindedness; the picture is complicated, during its development and course, by episodic states of depression and excitation.

At the onset, depressive symptoms usually predominate (insomnia, self-accusation, "blueness," unrest, suspicion, sense of change in things about him or in himself, ideas of reference). Illusions, hallucinations and delusions soon appear, the latter consisting chiefly of grandiose, or of persecutory, ideas. The delusions multiply rapidly, though the patient's recording faculty and orientation remain little disturbed. The gross irrationality of the delusions is characteristic, suggesting that of dementia paralytica (the universe has been cut out of his abdomen; his body has been cut apart and sewed together again; he is shut in a cell with an animal that has swallowed him). Delusional falsifications of memory are common;

the patient tells stories of marvellous experiences with great men, or of wonderful personal acts.

There is no disease-insight. The apathy and indifference are characteristic. The dementia progresses rapidly with the appearance of incoherence in speech and writing (confusional dementia). The patients show an especial tendency to print and to draw pictures.

**Differential Diagnosis.**—The diagnosis may be difficult at first, but is easy later on. The condition must be differentiated from (1) *chronic hallucinatory paranoia* (much slower course, delusions less gross and more systematized, dementing process less marked), and (2) *dementia paralytica* (age, somatic signs, lumbar puncture).

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## 4. The Infectious, Toxic, and Exhaustion Psychoses

Under this heading we usually include (1) the initial deliria, febrile deliria and convalescent deliria of the infections and intoxications, of

which those occurring in typhoid fever are the type, and (2) certain closely related states; (a) acute delirium, and (b) amentia, or acute hallucinatory confusion.

It was the infectious psychoses that first attracted attention to the close relation between internal medicine and psychiatry. In infectious diseases, delirium may appear at the beginning (initial delirium), or during the main course (febrile delirium), or in convalescence (defervescence delirium, inanition delirium, collapse delirium, exhaustion psychosis). These various forms of delirium are most often met with in typhoid, in influenza, in pneumonia, and in acute articular rheumatism (or its complications), or, they may occur in the course of any infectious disease. There need be no relation between the height of the fever and the intensity of the psychic symptoms.

### (*a*) *Initial and Febrile Deliria*

In the *initial* and the *febrile deliria,* the principal symptoms are (1) clouding of consciousness, (2) disorientation, (3) hallucinations; in addition, there may be (4) violent motor excitement, sometimes resembling that of mania, or (5) stuporous states.

### (*b*) *Collapse Delirium*

In the *deliria of convalescence* (collapse delirium, exhaustion delirium), the mental anomalies may appear suddenly, after the temperature has become normal. They consist of (1) dreamlike confusion, (2) hallucinations and illusions, (3) occasionally delusions, (4) lively motor excitement. The patients are usually anxious, suffer from self-accusation, ideas of sin and other micromanic delusions; sometimes, instead, the state may be euphoric. Stupor and excitation may alternate. In several cases I have observed catatonic phenomena (negativism, waxy flexibility), especially in pneumonia and in typhoid.

These collapse deliria may last a long time (weeks or months), though the outcome is usually favorable.

### (*c*) *Acute Delirium*

(*Delirium acutum*)

This name has been given to febrile deliria and to deliria occurring in the course of other psychoses, in which the agitation, confusion, and incoherence have been extreme. Sometimes there is muttering delirium with carphologia and sopor. The prognosis is grave.

### (*d*) *Acute Hallucinatory Confusion*

(*Amentia, Acute Confusional Insanity, Acute Hallucinosis*)

In various infections, intoxications, and states of exhaustion (especially after operations), an abnormal mental state may appear, characterized by (1) the sudden onset of dreamy clouding of consciousness; (2) numerous, and very lively, disconnected, hallucinations and delusions; and (3) peculiar motor symptoms, consisting either of increased impulse to movement, or stuporous inhibition (Siemerling). The patients are confused, disoriented and incoherent; the recording faculty is markedly disturbed; the mood is anxious and variable. Some of the psychoses of pregnancy and of the puerperal period belong here.

The patients usually emaciate rapidly, and they suffer from anemia, anorexia, and insomnia.

Amentia usually lasts from six to nine months, or even longer than a year. Many die from inanition or from complicating infections; some commit suicide; about one-third recover; a few go over into chronic mental disease.

**Differential Diagnosis.**—(1) From *manic-depressive states* (greater prominence of exaltation or depression; less confusion); (2) from *epileptic insanity* (history of fits; epileptic heredity); (3) from *catatonic form of dementia precox* (consciousness clear; presence of specific catatonic symptoms); (4) from *dementia paralytica* (somatic signs, lumbar puncture, Wassermann reaction).

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## 5. The Alcoholic Psychoses

Under this heading will be considered: (a) the mental anomalies of chronic alcoholism; (b) delirium tremens; (c) dipsomania; (d) Korsakoff's psychosis; and (e) paranoid states related to alcoholism.

### (*a*) *The Mental Anomalies of Chronic Alcoholism*

Men and women who become chronic alcoholics are usually especially predisposed by the inheritance of a bad nervous system, or by infantile

disease of the brain (meningitis, encephalitis, trauma). A drunkard cannot drink moderately, but is overcome by the irresistible impulse to drink excessively, even when he knows that drinking is injurious to his body and mind.

Regular drunkards usually pass through two stages: (1) that of apparent overnutrition, in which they look healthy, of good color, well nourished and strong; and (2) that of alcoholic cachexia, in which they are emaciated, pale, cyanotic, tremulous, and unsteady, present the Bardolphian facies, and are indifferent and incapable.

The psychic deterioration shows itself in (1) an ever-increasing irritability, especially when in association with the family; (2) progressive ethical deterioration (egoism, lying, indolence, indecency, loss of will-power); (3) intellectual deterioration (inability to concentrate, loss of memory, enfeebled judgment).

### (*b*) *Delirium tremens*

This form of delirium occurs in chronic drunkards, usually after many years of excess; it usually appears after a temporary abstinence from alcohol, due to gastric catarrh, to infection, or to lack of access to drink.

The delirium breaks out suddenly, lasts from two to ten days, and is characterized by a dreamy alteration of consciousness, with abundant hallucinations (particularly visual and kinesthetic) and illusions. The patients are especially prone to see a large number of small, moving, dark objects (flies, mice, lice, snakes, black dwarfs, etc.), and are usually completely disoriented. The mood is extremely variable. The patient may one moment be exalted and happy, and the next moment exhibit the signs of fear or of despair. Such patients are often violent, and may become a source of danger to those about them. One man who boarded a train at Baltimore for New York in an apparently normal state on entrance, shot a porter dead and threatened the whole car before reaching Wilmington.

Fever, tachycardia, anorexia, and sweating often accompany the attack, albuminuria and tremor always. At the end of the attack the patient, if he is to recover, falls into a deep sleep, and awakes with a clear consciousness, again fully oriented. Death may occur from heart failure, from a complicating pneumonia, or from gastro-intestinal catarrh.

**Differential Diagnosis.**—If the patient's habits are known, there is usually but little difficulty in arriving at the diagnosis. If not, delirium tremens may be confused with *other twilight states,* or *other deliria* (hysterical and epileptic twilight states; traumatic psychoses; infectious or toxic deliria).

### (*c*) *Dipsomania*

This has nothing to do with delirium tremens; it is probably a form of epilepsy. It is characterized by the periodic return of attacks in which

there is an irresistible impulse to excessive drinking, the impulse being attributed by the patients to an indescribable anxiety, an inexplicable restlessness, or to some unknown cause. In a given person, the recurring attacks resemble one another closely. After a single drink the patient begins to drink rapidly, without choice or purpose, though usually he takes whisky, brandy or gin. No matter what his circumstances are, he usually resorts to low dives or walks in the country from saloon to saloon until, finally, he is completely overcome by the intoxication. A single attack lasts, in most cases, about three days, but it may extend to a week or to two. The patient may be found by his friends in low resorts, or, returning to consciousness by himself, may apply to some hospital for treatment. Subsequent to an attack, the patient is depressed and self-accusatory; he resolves never to take another drink, and he may be industrious and abstinent until the occurrence of the next attack.

Cure is rare, though attacks may disappear for years, especially if the patient be kept in a closed institution for a time. After repeated dipsomaniac attacks the patient may begin to drink also between attacks, and become a chronic alcoholic. Emphasis is laid on the fact that dipsomania is not the result of chronic alcoholism, but is a sign of a periodically recurring mental anomaly.

### (*d*) *Korsakoff's Psychosis*

(*Polyneuritic Psychosis*)

This psychosis is most common in alcoholism, though it occurs in other conditions that give rise to multiple neuritis (*q. v.*). The same psychosis is sometimes met with, it is said, in the entire absence of neuritic phenomena.

The syndrome is usually easy to recognize, in that the patients exhibit a peculiar disturbance of memory, forgetting immediately all new impressions and the most recent events (from impairment of the recording faculty), though older memories remain and are worked up into pseudo-reminiscences or memory falsifications, leading the patient to describe experiences, adventures, travels and undertakings that have no basis in fact.

Cure is rare; chronic mental disease usually results.

### (*e*) *Paranoid States Related to Alcoholism*

In chronic alcoholism two varieties of the paranoid state are not infrequently met with: (1) the jealousy insanity of drunkards, and (2) an acute alcoholic paranoid state (see Paranoia acuta).

The jealousy delusion of drunkards develops with the deterioration of his ethical feelings, when the idea occurs to him that, owing to his own

frequent absence from home and his own increasing sexual impotence, his wife has occasion for amorous relations with others. The idea soon becomes transformed into a fixed delusion, and is supported by auditory and visual hallucinations. The wife is often violently mistreated, even murdered. The symptoms disappear after a few weeks of total abstinence in an asylum, only to reappear again, later on, when the drinking-habits are resumed.

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## 6. Psychoses Related to Drug Habits

The two drug habits most commonly met with by the practitioner are the morphin habit and the cocain habit; recently the heroin habit has become common, and has begun to supply its quota of the psychoses.

### (*a*) *The Morphin Habit and the Morphin Psychoses*

As with alcohol, certain people have nervous systems unable to resist the tendency to relieve discomfort or depression by morphin. It is especially common among those to whom morphin is easily accessible (druggists, physicians, veterinarians, trained nurses), though it sometimes develops in psychopathic patients following upon a morphin therapy. Husband and wife not infrequently become simultaneous victims. The hypodermic use is the most common.

Once established, the habit is very hard to break. Many hypodermics are taken secretly each day. If the physician suspect it, the patient should be undressed, when the numerous, small, pigmented spots, corresponding to the injection sites, become visible. A cachexia gradually develops, with sallowness and emaciation, and degeneration of the character (ethical defects, lying, egoism, loss of memory). Sudden abstinence may call forth alarming symptoms (restlessness, anxiety, despair, vomiting, delirium), quickly relieved by a hypodermic injection.

### (*b*) *The Cocain Habit and the Cocain Psychoses*

The deterioration in the cocain habit progresses more rapidly than with the morphin habit. Very frequently morphinism and cocainism are combined. In the cocain habit a psychosis of the type of acute hallucinatory confusion (amentia, *q. v.*) often develops. Abstinence phenomena in the

cocain habit are milder, and disappear more quickly, than in the morphin habit.

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## M. The Idiocies and Imbecilities (Dependent upon Faulty Development of the Brain)

Congenital feeble-mindedness is known in the milder cases as *constitutional inferiority,* or as *mental debility;* in the severer cases, as *imbecility;* the worst form, in which a mind, in the ordinary sense, can scarcely be said to exist, is *idiocy.* These conditions are sharply to be distinguished from dementia, or feeble-mindedness, acquired later on in life (dementia precox, dementia paralytica, alcoholic dementia, etc.).

The idiocies and imbecilities are nearly always organic diseases, due to faulty development or to early destruction of the cerebral neurons.

### 1. Imbecility

(*Congenital Feeble-mindedness*)

Human beings present every gradation in mental development from the highest endowment down to outspoken idiocy, and it is difficult to

draw a hard and fast line between normality and imbecility, for, owing to the great variations that exist, a normal state of mental life can scarcely be set up. The best that can be done is to make comparisons with the average capacity of other persons of the same age and social standing. A rough practical test consists in the ability independently to meet the world at the end of adolescence. Persons that are unable to "find their own way," exhibit, on analysis, defects of intellect, emotion or will, which account for the incapacity.

The laity have coined a series of names that are applied to imbeciles of various grades (eccentrics, originals, the simple-minded, the limited, blockheads, numbskulls, fools, dunces, no-goods, Weary-Willies, Simple-Simons, etc.).

Imbeciles are unable properly to perceive and properly to utilize perceptions, often owing to anomalies of attention, of interest, or of assimilation. They may have a fairly good recording faculty, learning things easily by heart (so-called mechanical memory), but they are unable to utilize their memories for making new arrangements (logical memory).

On the emotional side there is often a disproportion between the feelings and the stimuli arousing them, exhibiting itself either as abnormal excitations or as abnormal indifference. These persons are usually lacking in self-control, are hypersensitive, irritable, and prone to outbreaks of passion; or, on the other hand, they may be pathologically apathetic and stupid.

Often, in the "high-grade" imbecile, the narrow-mindedness, the limitation to concreteness, the inconsistency or dependency of their lives, the egoismus, the superstition, the preternatural suggestibility, and still other evidences of mental deficiency are recognizable.

Imbecility may not, like idiocy, be recognizable in early infancy, except, perhaps, in protraction of the time when the child learns cleanliness, or learns how to walk or to speak. The defect is often first recognized when the child goes to school, where he is backward, though in the studies in which learning by heart is the method used, the child's deficiencies may not be so evident as, later on, when logical thinking is necessary; then the defective judgment shows itself. The milder grades of imbecility may first reveal themselves in adolescence, in the lack of self-control with regard to the sexual feelings, or with regard to the use of alcohol, and the like. In the female sex it seems probable that a majority of prostitutes are somewhat imbecile.

It is customary to divide imbeciles into two great groups: the apathetic type (dullness, lack of interest, absence of initiative), and the erethic, or excitable, type (mobile, fanciful, active but superficial, illogical, vain, unsteady). The *apathetic type* may under strain, pass through episodic states of anxious confusion, with or without hallucinations and delusions. They may become prostitutes, drunkards, or tramps. From the *excitable*

*type* are recruited the pathological liars, the swindlers, the quacks, and the adventurers. The so-called *moral insanity* appears to be a form of imbecility, in which the chief defect is in a lack of the higher ethical and social feelings. These imbeciles are antisocial in nature. The term moral insanity is, however, a bad one, and has been used as an omnium gatherum to include not only (1) ethical imbeciles, but also (2) partial dementias following epilepsy or dementia precox, and (3) general degenerates, in whom there are bodily, intellectual, and emotional defects.

Many imbeciles are the victims of cerebral palsies (paralysis, contractures, speech disturbances, convulsive seizures, etc.), or show the somatic stigmata of degeneration (*q. v.*).

Of the developmental defects of the cerebrum that lead to imbecility may be mentioned (1) hemorrhages, (2) encephalitis, (3) internal hydrocephalus, (4) meningitis, and (5) porencephaly. In some families imbeciles crop out singly through a series of generations, suggesting mendelian heredity—the presence, or absence, of some mendelian unit (Goddard, Davenport). Chronic alcoholism, or lues, in one or both parents seems to have been responsible in some cases.

**Diagnosis.**—Two points have to be considered: (1) the demonstration of feeble-mindedness; (2) the proof that this has been congenital, or infantile, in origin, rather than evidence of a dementia having its origin in later life.

The possibility of an existing myxedema, cretinism, mongolism, or infantilism should always be kept in mind.

A systematic psychic examination of the cognitive, affective and conative functions (intellect, emotion, will) is necessary, in order that the mental equipment of the suspected imbecile may be compared with the average equipment of a healthy person of the same age and social position. The anamnesis usually suffices for the decision as to whether the feeble mind is congenital or is a dementia resulting from disease acquired later on. In imbecility, certain faculties will never have developed; in dementia, traces of faculties that have been previously developed will be discoverable.

The Binet-Simon tests are here very helpful, provided not too much is expected of them.

It is desirable to test (1) the gnostic intelligence (tactile agnosia, acoustic agnosia, optic agnosia, illusions, hallucinations); (2) the symbolic intelligence (sensory aphasias, amusias, inability to understand numbers, symbols, signs); and (3) the practical intelligence (motor aphasias, apraxias, power of calculation). Heilbronner's figures for testing symbolic intelligence are useful.

## 2. Idiocy

Here the mental defect is so outspoken that even the laity recognize it, whereas in mild imbecility even the expert psychiatrist may sometimes be in doubt. Various grades of idiocy exist, and there is every transition through the milder forms to mere imbecility.

The lowest idiots resemble animals deprived of a cerebrum. They are vegetative, reflex machines (Hoche), with apparently no mental life; and they usually, fortunately, die early. Above these are the idiots that are capable of expressive movements, who manifest their pleasures and their pains, exhibit defensive movements and certain automatic movements (rubbing, rotating, shaking, etc.). Though they are capable of sense perception, they have no capacity for close attention, and new sensations, apparently, do not call up old experiences. Such idiots are not educable. Higher idiots may learn a defective kind of speech (incorrect grammar, abnormal articulation), and can make themselves understood regarding their bodily needs and their pleasures and pains. They may become oriented as to place and persons, and can be taught certain habits of cleanliness and of behavior, but they are incapable of school education. Forms of congenital defect above this level are classed as imbecility.

Fig. 631.—Mongolian Idiot. Age One Year. Note Oblique Lid Slits, Thick Lips and Tongue, Salivation. (After M. Pfaundler in E. Feer's "Lehbrb. d. Kinderheilkunde," published by G. Fischer, Jena.)

Idiots, like imbeciles, are divisible into (1) apathetic, anergetic, or torpid, and (2) excitable, energetic, agile, or versatile types. Some of them are good-natured; others are ill-natured and irritable. Most idiots show organic nerve lesions (paralyses of limbs or of the eye-muscles, athetosis), or anomalies in the shape of the skull (secondary to cerebral anomalies?). Stigmata of degeneration are common. About one-third of all idiots have epilepsy.

**Pathology.**—Leaving out the thyreogenous idiots, most idiots are such because of primary encephalopathies. These include the porencephalies, cysts, tuberous scleroses, lobar scleroses, microgyries, microcephalies, and hydrocephalies.

**Diagnosis.**—The only difficulty lies in delimiting idiocy from imbecility in cases on the borderline. The line is arbitrary, and practically insignificant. Seen late in life, in the absence of a history, one may be in doubt whether he is dealing with idiocy or with an extreme dementia in a late stage of dementia precox or of dementia paralytica. Exact examination, however, quickly reveals, as a rule, the condition.

Idiots are "irresponsible." They may be thieves, incendiarists, rapists, but the "criminal group" is recruited from imbeciles rather than from idiots. The internist can do much to protect, if he care to, microcephalic idiots from skull operations, to which the hopes of fond but ill-advised parents and the zeal of insufficiently experienced surgeons sometimes impel.

**Mongoloid Idiocy.**—This condition first recognized by Down (1866), is now a well-recognized form. The child has a peculiar physiognomy, which has led to the name mongoloid; the "face is flat, the dorsum nasi broad, the malar bones prominent, the eye-slits narrow and oblique, the eye-lids reddened with scanty cilia, the cheeks greyish brown, tinted with red, suggestive of the make-up of a clown, the skull round, the occiput flattened." The tongue is enlarged and has huge circumvallate papillae; the dorsum of the tongue is wrinkled and looks like the surface of the scrotum (*langue scrotale*). The musculature is relaxed and soft and the joints can be twisted in remarkable attitudes ("snake-baby"). Many malformations throughout the body have been observed in different cases of mongolism.

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# Part XIII

# Diagnosis of the Disorders of Metabolism

SECTION I

THE PRINCIPLES OF NUTRITION AND THE METHODS OF INVESTIGATING METABOLISM

## A. General Introduction to the Study of Metabolism

### 1. The Nature of Metabolic Processes and Some of the Applications of a Knowledge of Metabolism

#### (*a*) *Definition of Metabolism*

By the study of metabolism we mean the investigation of the changes that substances introduced into the body undergo while passing through it, or on becoming incorporated in it, and the transformations of energy that accompany these processes.

#### (*b*) *Metabolism in Plants and in Animals*

The metabolism of animals differs somewhat from that of plants. In the **plant,** the light and heat of the sun, with the help of the chlorophyll of the green leaf, causes carbon dioxid taken from the air, and water drawn up from the roots, to unite and form sugar—a *synthetic process,* and during this process heat is absorbed and oxygen is given off into the atmosphere. The actual energy from the sun is converted into the potential energy of sugar. If the sugar be burned in a bomb calorimeter with oxygen under pressure, carbon dioxid and water will be formed again, and precisely the same amount of heat will be liberated as was required for the

original synthesis. The processes of vegetable growth are largely *reduction-processes.*

In contrast with this is the metabolism of the **animal** body, in which highly complex molecules that have resulted from the synthetic work of plants are disintegrated into smaller molecules by processes of *cleavage* and of *oxidation,* with formation of carbon dioxid and water.

As a matter of fact, whereas synthetic processes predominate in plants, and processes of cleavage and oxidation predominate in animals, both sets of processes occur in each of these kingdoms. We now know, for example, that very important synthetic processes occur in the animal body. Even the complex proteins of plants, or of animals, when taken into the human body are disintegrated into relatively simple constituents (*amino acids*), which are resynthetized into proteins peculiar to the human species. In addition to proteins, many simpler substances are synthesized in the human and animal body. I may refer to the well-known synthesis of urea (from $CO_2$ and $NH_4OH$) in the liver, and of hippuric acid (from benzoic acid and glycocoll) in the kidney.

### (c) *Matter and Energy in Metabolism*

Of the substances taken into the human body as food and drink, part are used up for the growth and maintenance of the protoplasm of the body tissues, which are all the time breaking down with loss of substance that must be replaced, and part leave it (in an altered or unaltered state) in the form of secretions or of excretions. Thus, the **matter** of which the body is composed is continuously undergoing change. Substances are constantly coming in and substances are constantly going out, a process well described by the German *Stoffwechsel.*

But, in addition to the changes in matter, we must consider the changes in **energy.** If we contrast the intake with the output, we find that the potential energy of the former is very much greater than the potential energy of the latter. For a great deal of the *potential energy* of the intake is converted within the body into *actual energy,* appearing as *heat,* the mechanical *work* of muscle contraction, and *electricity.*

Lavoisier long ago showed that, on oxidation of an organic substance, the products of combustion are equal to the sum of the original substance and the oxygen used. It was he who proved that animals and men absorb oxygen and eliminate carbon dioxid, just as does a burning piece of wood. He even measured the heat given off by a guinea-pig by recording the quantity of ice melted when the animal was placed in a hollow block of ice. He measured the gases given off by the animal to see whether or not the heat produced was accounted for by the oxidation that went on inside. He found that the amount of oxidation in the human body was greater after the ingestion of food, after muscular exercise, and after exposure to cold. He was wrong, however, in thinking that the heat production is due to oxidation of carbon and hydrogen in the lungs, and it was not until more than half a century later that it became clear that the production of heat in the animal body depends upon the oxidation of protein, fat and carbohydrate within the cells of the different organs of the body. Since Lavoisier's time, a vast deal has been learned regarding the processes of metabolism.

Thanks to the studies of Abel, Atwater, Benedict, Chittenden, Dakin, Folin, W. Jones, Levene, Lusk, McLeod, Mendel, Osborne, Wells, Woodyatt and others in this country, of Bancroft, Cathcart, Funk, Garrod, Halliburton, Hopkins, Pavy, Plimmer, Starling and Schaefer in England, and of Voit, Rubner, Emil Fischer, Kossel, Schmiedeberg, von Noorden, Friederich von Müller, Abderhalden and Umber in Germany, to say nothing of the work of French, Italian, Russian and Scandinavian workers, metabolic studies have made, and are making, very rapid progress.

The foundation of the modern doctrines of metabolism is the discovery that the **law of the conservation of energy** holds for the changes that take place in the animal body, as well as for all other processes.

In studying the metabolic processes, we have learned to consider, therefore, both the material (or chemical) side, and the dynamic (or energetic) side, and the two methods of consideration supplement one another. On the material side, we study the chemical changes that the single substances taken in as food undergo, and the intermediary stages through which they pass before their end-products are eliminated from the body. On the dynamic side, we consider the potential energy of the elements of the food intake, and the potential energy still remaining in the constituents of the output (urine, feces, etc.); subtracting the latter from the former, we have the amount of potential energy that has been either stored up in the body or converted within the body into actual energy (heat, mechanical work, electricity).

A remarkable feature of the **oxidative processes** within the body is the fact that substances, which can be easily oxidized in the test tube, may leave the body before having undergone complete oxidation, while, on the other hand, substances such as fats, which are difficult to oxidize in the test tube, are easily burned completely within the animal body, with formation of carbon dioxid and water. We now know that these processes of combustion go on chiefly as a result of the catalytic action of *ferments* within the *cells* of the various organs of the body, each little cell being a chemical laboratory with processes peculiarly its own. The characters and intensities of the process in each cell depend in part upon the materials that reach it (through the blood and lymph), in part upon the rapidity with which the products of its chemical activity are removed from the cell, and in part (a very large part) upon the varying need of energy, by the body, for the processes of its life. As Rubner has emphasized, the body cells are capable of adapting themselves in a remarkable way to the claims made upon them. The chemistry of a given person varies greatly under different circumstances (rest, work, temperature, climate, disease). It is not so much the amount of protoplasm that determines the total quantity of change or the rate of change; it is the amount of "life" that is decisive.

### (*d*) *The Chemical Nature of the Food Ingested*

The intake of food and drink consists partly of **organic substances** (*proteins* and their derivatives; *nucleins* and *purins* and other nitrogenous substances; *carbohydrates; fats; lipoids*), and **inorganic** or **mineral substances** (*salts* and *water*). The body is, on the one hand, in constant need of substances to replace parts of its machinery lost in wear and tear, and, on the other, in constant need of fuel to supply the potential energy for conversion into the actual energy of the body. For the former purpose, protein is essential; for the latter purpose, carbohydrates and fats are most important, though proteins also contribute to the fuel value of the food. In addition to protein and fuel, the body requires salts and water, partly for the maintenance of the machinery, and partly to supply the conditions necessary for the conversion of potential into actual energy, especially for the maintenance of the osmotic processes in the organism so important for absorption and secretion.

Recently, the necessity of the presence of certain peculiar substances in the intake, the nature of which is not yet definitely known, has been demonstrated. These substances, known at present as **vitamins,** will be referred to further on.

### (*e*) *The Potential Energy, or "Fuel Value," of the Food Ingested*

The amount of potential energy in the food intake can be directly determined by measuring the heat given off on its combustion. As a *unit of measurement* we make use of the **large calorie** (Cal.), that is, the amount of heat necessary to raise the temperature of one kilogram of water from 0° to 1° C.

When one gram of *glucose* is burned in a bomb calorimeter, it yields heat sufficient to raise the temperature of one liter of water 3.755°; that is, 1 gram of glucose yields 3.755 calories of heat. When *protein* is burned in the bomb calorimeter, its nitrogen is oxidized to nitric acid, but when protein is burned in the body, the nitrogen is eliminated in the form of urea, a substance that is not fully oxidized. Moreover, a certain small amount of the protein ingested is given out in the feces unoxidized, or only partially oxidized. Since protein is, therefore, less fully oxidized in the body than in the bomb calorimeter, the heat produced from protein in the body is always somewhat less (about 25 per cent less) than that measured in the bomb. *Sugars* and *fats,* when oxidized in the body, yield the same products, and exactly the same amount of heat, as when oxidized in the bomb.

The **physiological heat value** of ordinary food stuffs, when oxidized in the body, is as follows:

| | | Calories |
|---|---|---|
| 1 *g.* | Glucose | 3.755 |
| 1 *g.* | Cane sugar | 4.0 |
| 1 *g.* | Starch | 4.1 |
| 1 *g.* | Fat | 9.3 |
| 1 *g.* | Protein | 4.1 |
| 1 *g.* | Alcohol | 7.0 |

With the aid of these figures it is easy to *calculate the fuel value,* for the body, of any food taken in. Thus, if we know the quantity of protein, fat and carbohydrates ingested in 24 hours, we can calculate the quantity of heat that, in health, will arise from its oxidation within the body. Elaborate tables giving the protein, fat, and carbohydrate content of ordinary foods are available. If the food intake of a given person for 24 hours consist of 100 grams protein, 100 grams fat, and 400 grams carbohydrate, the quantity of heat resulting will be as follows:

| | | | Calories |
|---|---|---|---|
| 100 *g.* | Protein | 100×4.1 | 410 |
| 100 *g.* | Fat | 100×9.3 | 930 |
| 400 *g.* | Carbohydrate | 400×4.1 | 1,640 |
| | | | 2,980 |

Rubner proved that if an *animal* be placed in a calorimeter, which measures the heat actually given off during a period, the value found corresponds exactly to the calculated value. And in the United States, Atwater, Rosa and Benedict, by means of a large calorimeter constructed to measure the heat production in *man,* confirmed the application of the law of the conservation of energy to the human species.

To show how accurately the heat produced may be theoretically calculated, the results of investigations made under Lusk's supervision in the calorimeter of the Russell Sage Institute of Pathology in Bellevue Hospital may be cited. In a lamp within the apparatus, a definite amount of alcohol was burned during a four-hour period. Theoretically, the fuel value of the alcohol was 212.57 calories. The heat actually produced and measured was 211.88 calories.

A patient suffering from typhoid fever was placed in this calorimeter and studied while at rest for a period of five hours by DuBois and Coleman. Theoretically, the heat production in this man's body should have been 422.59 calories; the amount of heat actually measured was 419.78 calories.

Rubner showed that the different organic food substances can, to a certain extent, as far as their fuel value is concerned, replace one another according to what he has called the **isodynamic law.** Thus, 9.3 grams carbohydrate and 4.1 grams of fat are isodynamic equivalents; in other words, 1 gram of fat is equivalent in fuel value to 2.3 grams of carbohydrate. But the isodynamic law does not hold for protein. A certain amount of protein is absolutely essential in the food, as we shall see later, and cannot be replaced by any other substance.

### (*f*) *Applications to Dietetics*

In **practical dietetics,** many points have to be considered, but the two points of prime importance are (1) the *fuel value* of the food, and (2) the presence of *sufficient protein* and of *sufficient vitamins.*

**Heat Production in Man.**—The quantity of heat produced by mamma-

lian animals, including man, can be closely predicted in advance. It varies considerably, according to the animal species; for instance, a mouse requires thirty times more food per unit of body weight than the horse, though the single cells in the mouse are of about the same size as the cells in the horse. The fuel value of the food required is thus seen to depend neither upon the weight of the animal nor upon the relative size of the single cells. It does stand in a constant relation, however, to the *extent of the surface of the body;* all well-nourished mammals produce the same number of calories per square meter of surface (Rubner).

**Heat production** (the fuel value of the food required) for man varies, (1) according to the *size of his surface,* and (2) according to the quantity of *mechanical work done. Age, external temperature* and *disease* are also of influence.

**Basal Heat Production.**—A normal man, if well nourished, and remaining quietly at rest in bed in the morning, having been without food for fifteen hours, will produce a minimal amount of heat (so-called **rest starvation value** or **basal heat production**). This basal heat production for a man of average weight (70 kilograms, 156 pounds) is about 70 calories per hour, or 1,680 calories in the twenty-four hours.

**Maintenance Requirement.**—If, now, the man eat food, extra heat is produced, which does not, however, exceed 10 per cent of the basal heat production (that is, 7 calories per hour, or 168 per day). The "maintenance requirement" of such a man, resting quietly in bed, would, therefore, be met by a daily diet having a fuel value of 1,848 calories (Lusk).

**Requirement When at Work.**—Beyond this "maintenance requirement," the amount of fuel needed will depend upon the quantity of **mechanical work** performed.

Lusk gives the following data as the best available at present for the estimation of the daily fuel requirement of well-nourished adults:

| | Calories |
|---|---|
| In bed 24 hours | 1,680 |
| In bed 8 hours, "work" involving sitting in a chair 16 hours | 2,170 |
| Bed 8 hours, in a chair 14 hours, moderate exercise 2 hours | 2,500 |
| Farmers | 3,500 |
| Rider in a six-day bicycle race | 10,000 |

An ordinary business man, or a clerk, or a man employed in watching machinery, requires, therefore, about 2,500 calories per day.

**Requirement in Childhood.**—The *new-born baby* requires at first 100 calories per kilo of body weight per day; later on 70 calories are sufficient. A *boy of twelve* requires a total of some 1,500 calories per day.

**Requirement in Disease.**—In *diseased conditions,* metabolism may be either accelerated or retarded. Thus, in **fever,** the heat production may be 50 per cent higher than normal. In **Graves' disease,** in which the thyroid gland is over-active, the heat production may be still higher. In

**myxedema,** and in cases of **constitutional obesity,** the heat production is much less than normal.

**Caloric Equilibrium and Disequilibrium.**—We speak of *caloric equilibrium* when the diet has a physiological fuel value that exactly *equals* the expenditure of energy by the body. On such a diet the patient's weight remains unchanged.

When the caloric intake *exceeds* the body need, the body weight increases, usually owing to increase in the amount of body fat.

If the caloric intake be *less* than the body need, the body will burn its own material and will decrease in weight. In this event, fat will be the first substance to be reduced in amount.

Though, in **arranging a diet,** the *caloric value* is an essential to be considered, it must be remembered that other points are also essential; namely, the supply of sufficient *protein* of the right quality, an adequate content of *water, salts* and *vitamins* in the diet, and attention to the *preparation of food* so that it shall be properly cooked and appetizing. We shall discuss some of these points further on.

**Habits of Diet.**—The habits of diet in different parts of the world are very diverse; thus, the diet of **Eskimos** is almost entirely *carnivorous,* consisting chiefly of seal meat, the meat of reindeer, walruses, whales, fish, blubber (fat) and native vegetables (huckleberries, angelica shoots, seaweed).

Among **Oriental peoples,** the staple diet is largely *herbivorous,* consisting of rice and a little fish. Some of the poor people in the Philippine Islands live on a diet that costs about 6¼ cents per person per day.

The *standard diet* for the **European laboring man,** as laid down by Voit, contains 118 grams of *protein,* 56 grams of *fat,* and 500 grams of *carbohydrate;* a little more than one-third of the protein is furnished in 230 grams, or half a pound, of butcher's meat.

The diets of the Eskimo, the Bengali and the laboring man in Europe when compared, show the following distribution of the various nutritive elements:

| | Weight in kgm. | Protein grams. | Total Calories | Calories in Per Cent | | |
|---|---|---|---|---|---|---|
| | | | | Protein | Fat | Carbohydrates |
| Eskimo..... | 65 | 282 | 2,604 | 44 | 48 | 8 |
| Bengali..... | 50 | 52 | 2,390 | 9 | 10 | 81 |
| European..... | 70 | 118 | 3,055 | 16 | 17 | 67 |

It will be seen that the Eskimo takes five times the amount of protein eaten by a Bengali, and 2½ times the amount eaten by a European, and yet, according to Krogh, he does not suffer from gout. The Eskimo's diet enables him to bear extreme cold.

**Voit's diet** (see above) has been greatly criticized as financially extravagant and as physiologically harmful. Chittenden, in a series of important investigations, has studied the **protein minimum** upon which nitrogen equilibrium can be maintained and finds it very much lower than was formerly supposed, but Meltzer points out that eating protein in quantities above the minimal required amount is to be regarded as one of the many "**factors of safety**" in human life. The minimal amount of protein that will maintain nitrogen equilibrium is by no means the **optimal amount of protein** for the welfare of a person.

Rubner, in Germany, is an advocate of a high protein intake, and Lusk and a number of other authorities on metabolism in the United States believe that a liberal meat diet for the people at large is beneficial. *I would warn, therefore, against the reduction of protein to too low a figure, and also against the too free use of inferior proteins at the expense of the superior proteins* (see Protein Metabolism).

**Economic Importance.**—A knowledge of the main facts of metabolism is of real economic importance for the people of a country. Graham Lusk is doing an important service in educating the people of the United States regarding the monetary value of foods. Realizing that it is "of no small moment that the citizen should know how best to maintain the machine at a maximum of efficiency" and "where to turn to find nourishment in the form that is best and cheapest," he has published an article in the *New York Evening Post*, entitled "Food at Fifty Cents a Day," and a little volume called "The Fundamental Basis of Nutrition," in which, in simple language, the main facts are discussed. The excellent article of Murlin in the *Popular Science Monthly* has also been written with similar intent.

**The Cost of Living.**—To provide a diet for a family of five (father, mother and three children, without servants), some 7,750 calories per day are required, 5 per cent of which should be in normal proteins of Grade A, and 10 per cent in vegetable proteins of Grade C (bread). The cost, according to Lusk, in the New York market in January, 1913, would be as follows:

| | Cents |
|---|---|
| Bread + $\frac{4}{5}$ pound salt cod | 47 |
| Bread + $\frac{2}{5}$ pound smoked ham | 48 |
| Bread + $\frac{4}{5}$ pound cheese | 51 |
| Bread + 2½ pounds milk | 53 |
| Bread + 1½ pounds loin pork | 56 |
| Bread + 1⅓ pounds leg of mutton | 56 |
| Bread + 1¼ pounds cod steak (fresh) | 58 |
| Bread + 1⅓ pounds sirloin beef | 66 |
| Bread + 1½ pounds turkey | 78 |

The cost of the food for an adult requiring 2,500 calories would be one-third the cost for the family, and this cost would not exceed 20 cents a day at the market price of the fresh materials. Lusk estimates that

"when more than an average of 8 cents is expended for 1,000 calories of nutriment, the diet must include luxuries."

The following table, also taken from Lusk, represents the market price in cents of 1,000 calories in various staple foods:

*Cost in Cents of 1,000 Calories*

| | |
|---|---|
| Glucose | 1⅔ |
| Cornmeal | 2 |
| Wheat flour | 2½ |
| Oatmeal | 2⅘ |
| Cane sugar | 3⅓ |
| Dried beans | 4 |
| Salt pork (fat) | 4½ |
| Rice | 5 |
| Wheat bread | 5⅓ |
| Oleomargarine | 7½ |
| Potatoes | 7½ |
| Butter | 10 |
| Milk | 10 |
| Smoked ham | 10¾ |
| Cheese | 11⅔ |
| Loin of pork | 12¼ |
| Mutton (leg) | 16¼ |
| Salt cod | 19½ |
| Sirloin steak | 24 |
| Turkey | 40 |
| Codfish steak (fresh) | 42 |

If the family of five above referred to should keep a servant, 30 per cent more food is required. It is said that three servants will double the food bill, and six will triple it.

The household requirements for families of different degrees of income can, according to Lusk, be formulated as follows:

| | Calories | Cost in Cents | |
|---|---|---|---|
| | | Minimum | Maximum |
| Poor family | 7,750 | 50 | 70 |
| Well-to-do | 15,500 | 100 | 140 |
| Wealthy | 23,250 | 150 | 210 |

Any money spent "above these amounts is paid for waste or for non-essentials in the form of flavors of high price."

The physiological value of portions of food sold over the counter of Childs' Restaurants in New York has been studied by F. C. Gephart of the Russell Sage Institute of Pathology. For comparative standards, the calories in bread and vintage champagne purchased elsewhere were selected. The following table, taken from Lusk's monograph, shows a few of the results:

FOOD VALUE OF PORTIONS, IN CHILDS' RESTAURANTS, INCLUDING BREAD AND BUTTER WHEN SERVED

| | Cost in Cents | Calories | | Calories for Five Cents | Cost in Cents per 1,000 Calories |
|---|---|---|---|---|---|
| | | Total | Per Cent in Protein | | |
| Bread[1] | 5 | 933 | 12 | 933 | 5 |
| Apple pie | 5 | 337 | 5 | 337 | 15 |
| Boston pork and beans | 15 | 828 | 12 | 276 | 18 |
| Ham sandwich | 5 | 170 | 20 | 170 | 30 |
| Corned beef hash | 15 | 507 | 14 | 170 | 30 |
| Beef stew | 15 | 461 | 25 | 154 | 32 |
| Club sandwich | 25 | 409 | 20 | 82 | 61 |
| Sliced pineapple | 5 | 36 | 46 | 36 | 138 |
| Tomatoes, lettuce, mayonnaise | 20 | 53 | 16 | 13 | 385 |
| Pint of champagne[1] | 200 | 345 | 0 | 9 | 588 |

[1]Not purchased in the restaurant.

As Lusk points out, the table proves that Childs' Restaurant is by no means a charitable undertaking, but rather an institution for men of moderate means, if it be recalled that the average workman need not expend more than 8 cents per 1,000 calories of energy.

**What the Government Might Do.**—The Government might, advantageously, take up the matter of educating the people as to the most economical way to live. Each package of foodstuffs offered for sale might have on its label information regarding (1) the fuel value of the food in calories, and (2) the relative content of the food in protein, carbohydrate and fat. Care should be taken, however, not to give a false impression to the people. They may easily get the idea that fuel value is the only important thing in food. *Though the fuel value of a diet is very important, qualities other than the fuel value must not be neglected.* Among these, protein-content, variety of protein, and flavor are well worth paying for.

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# 2. The Metabolism of Proteins and Their Derivatives

## (a) *The Significance of Proteins in Metabolism*

The most important constituent of the protoplasm of all tissue cells is protein. A little of this protein is constantly being used up, so that, continuously, more protein must be supplied to the body cells. But aside from its use for the *repair of the "machinery,"* protein is also of importance in body metabolism as a *carrier of potential energy.*

In addition to the C, H and O that protein contains, in common with carbohydrate and fat, this foodstuff also contains N. In order that the study of the metabolism of proteins may be intelligently approached, the main facts of the physiological chemistry of proteins and their derivatives should be reviewed. A brief epitome follows.

## (b) *Résumé of the Physiological Chemistry of the Proteins*

Protein substances are characterized by *large molecules,* and solutions of proteins, accordingly, present *colloidal characters* (coagulability on heating; precipitation by concentrated salt solutions). Each molecule consists of a **long chain of rather simple chemical links.** The links differ qualitatively, and more especially, quantitatively, for the chains representing different substances, but these chains can be broken apart by *hydrolysis with acids,* or by the *action of digestive ferments* or *proteases* (pepsin, trypsin, erepsin), when the links are found to consist of **amino acids** of different sorts. These amino acids include both *monoamino acids* and *diamino acids.* Part of them belong to the fatty acid series, part to the benzene series, and a few contain heterocyclic nitrogenous ring systems. The proteins thus contain N, besides C, H and O, and also, nearly always S.

The great class of proteins may be roughly subdivided into groups as follows:

### i. The Proteins Proper

1. **The Albumins** (*e. g.,* serumalbumin, ovalbumin), soluble in water and in dilute salt solutions. Neutral in reaction. Not precipitated by acids or alkalis

in aqueous solution; precipitable, however, from strong salt solutions (NaCl; $MgSO_4$) by traces of acid. Not precipitable by $(NH_4)_2SO_4$ except in complete saturation. Contain no glycocoll, but rich in sulphur (1.5-2 per cent).

2. **The Globulins** (*e. g.,* serumglobulin, fibrinogen, thyroglobulin), insoluble in water; soluble in neutral salt solutions of medium strength; hence precipitable on dialysis. Soluble in dilute alkalis; on neutralization, precipitated unchanged, unless the amount of salt formed suffices to hold the substance in solution. They are precipitable from solutions by dilute acids, and by $CO_2$. They are acid in character. They are also precipitable by concentrating neutral salts in their solutions; viz.: on complete saturation with NaCl or $MgSO_4$, on half saturation with $(NH_4)_2\ SO_4$. They are easily "denatured" so as to become insoluble.

3. **The Muscle Proteins** (*e. g.,* myosin, myogen).

4. **The Scleroproteins or Albuminoids** (*e. g.,* kollagen, glutin, keratin, elastin, fibroin).

5. **The Histons and Protamins** possess an outspoken basic character, owing to the large amounts of arginin they contain.

### ii. The Compound Proteins (=Proteids)

These consist of *proteins proper* to which a so-called *"prosthetic" group,* of wholly different structure, is attached. Examples of such prosthetic groups are (1) pseudonuclein, (2) glucosamin, (3) nuclein, (4) hemochromogen.

The proteids include therefore:

1. **The Phosphoproteids** (*e. g.,* casein, vitellin). These were formerly called *nucleoalbumins,* a bad name, since they are not at all like the nucleoproteids of cell nuclei. They contain no nucleinic acid, though they are acids containing *P* in the prosthetic group (called *pseudonuclein*).

2. **The Glycoproteids** (*e. g.,* mucin, chondromucoid, seromucoid, etc.). In urine, a "urinary mucoid" occurs; it gives rise to the so-called nubecula. Acetic acid precipitates it. The glycoproteids are a combination of *protein* and *glucosamin.*

3. **The Nucleoproteids** (*e. g.,* nucleoproteids of thymus, pancreas, etc.). They consist of protein combined with animal nucleic acid, the latter in turn containing purin bodies, pyrimidin bodies, and a hexose combined with *P.* Plant nucleic acid has a somewhat different structure (*q. v.*).

4. **The Chromoproteids** (*e. g.,* oxyhemoglobin and its derivatives). These are combinations of a *protein* (globin) with the prosthetic group *hemochromogen* or *hematin,* a pyrrol derivative (of the heterocyclic series).

### iii. Degradation Products Derivable from Proteins

As has been said above, proteins consist of **chains of amino acids,** the carboxyl group—COOH—of one being united with the *amino group*—$NH_2$—of its neighbor in the so-called **"peptid bond"** (acid-amide-anhydride bond), with elimination of water, thus:

$$-CO\ \boxed{OH + H}.\ NH_2-$$
$$=-CO-NH_2-+H_2O$$

Now, on hydrolysis (by boiling with acids, or by the action of the ferments known as proteases), these chains of amino acids can be again split up, the cleavage occurring at the "peptid bond," with re-introduction of water, thus:

$$\begin{matrix} -CO-NH- \\ OH/\ \ \backslash H \end{matrix} \quad = COOH + NH_2-$$

In the course of **protein hydrolysis**, at least *four stages* are distinguishable:

I. *Stage of acid albumins or alkali albuminates,* the first cleavage products.

II. *Stage of albumoses (proteoses) and peptones,* a complex mixture of polypeptids of varying size and character. None coagulates with heat. All yield the biuret reaction. The albumoses and peptones are distinguished by the fact that the latter are not precipitable by $(NH_4)_2SO_4$.

III. *Stage of polypeptids* of smaller size.

IV. *Stage of end-products* (amino acids).

### 1. *The Amino Acids*

The principal amino acids thus far isolated are the following:

A. Amino Acids of the Fatty Acid Series.

I. *Monamino-monocarbonic acids.*

1. **Glycocoll** (glycin, amino-acetic acid) = $NH_2\,CH_2.\,COOH$.
2. **Alanin** ($\alpha$-aminopropionic acid) = $CH_3.\,CHNH_2.\,COOH$.
3. **Valin** ($\alpha$-amino-iso-valerianic acid) = $(CH_3)_2CH-CH.\,NH_2-COOH$.
4. **Leucin** ($\alpha$-amino-isobutyl-acetic acid) = $(CH_3)_2CH-CH_2-CH.\,NH_2-COOH$.
5. **Isoleucin** ($\alpha$-amino-$\beta$-methylethyl-propionic acid) = $CH_3.\,C_2H_5.\,CH-CH.\,NH_2-COOH$.

II. *Monamino-dicarbonic acids.*

1. **Aspartic acid** (aminosuccinic acid) = $COOH-CH_2-CH.\,NH_2-COOH$.
2. **Glutamic acid** ($\alpha$-aminoglutaricacid) = $COOH-CH_2-CH_2-CH-NH_2-COOH$.

III. *Diamino-monocarbonic acids.*

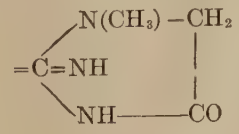
1. **Ornithin** ($\alpha$-$\delta$-diamino-valerianic acid) = $CH_2.\,NH_2-CH_2-CH_2-CH.\,NH_2-COOH$.
2. **Lysin** ($\alpha$-$\epsilon$-diamino-caproic acid) = $CH_2.\,NH_2-CH_2-CH_2-CH_2-CH.\,NH_2-COOH$.

IV. *Guanidino acids.*[1]

1. **Arginin** ($\alpha$-amino-$\delta$-guanidino-valerianic acid) = $NH_2-C(NH)-NH-CH_2-CH_2-CH_2-CH.\,NH_2-COOH$.

[1] Two substances related to these acids are:

*Creatin* (methyl-guanidino-acetic acid) = $NH_2-C(NH)-N(CH_3)-CH_2-COOH$ and *Creatinin* (methyl-glyko-cyamidin), not really an amino acid but an anhydride of creatin.



V. *Amino-oxy acids.*

1. **Serin** ($\alpha$-amino-$\beta$-oxypropionic acid) = $CH_2OH-CHNH_2-COOH$.
2. **Diamino-trioxydo-decanic acid.**

VI. *Sulphur-containing amino acids.*

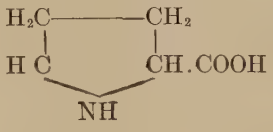
1. **Cystin** ($\alpha$-diamino-$\beta$-dithio-dilactyl acid) = $COOH-CHNH_2-CH_2.S-S.CH_2-CH.NH_2-COOH$.

B. Amino Acids of the Aromatic Series.

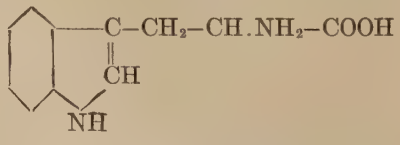
1. **Phenylalanin** (phenyl-$\alpha$-amino-propionic acid) = $C_6H_5-CH_2-CH.NH_2-COOH$.
2. **Tyrosin** (para-oxy-phenyl-$\alpha$-amino-propionic acid) = $C_6H_4.OH-CH_2-CH.NH_2-COOH$.

C. Amino Acids of the Heterocyclic Series.

1. **Prolin** ($\alpha$-pyrrolidin-carbonic acid) =



2. **Oxyprolin** (oxy-$\alpha$-pyrrolidin-carbonic acid).
3. **Tryptophan** (indol-amino-propionic acid) =



4. **Histidin** ($\beta$-imidazol-$\alpha$-amino-propionic acid) =

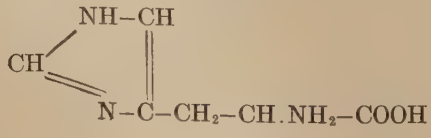


**Table Showing the Percentages of the Various Amino Acids in Several Proteins**

| | Serum Albumin | Serum Globulin | Bence-Jones Body | Casein | Fibrin | Thymushiston | Globin from Hemoglobin | Keratin | Elastin | Gelatin | Fibroin | Amyloid |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Glycocoll | 0 | 3.52 | 1.7 | 0 | 3.0 | 0.5 | 0 | 0.34 | 25.75 | 16.5 | 36.0 | 0.8 |
| Alanin | 2.7 | 2.22 | 4.5 | 0.9 | 3.6 | 3.5 | 4.29 | 1.2 | 6.6 | 0.8 | 21.0 | .... |
| Aminovalerianic acid | .... | .... | .... | 1.0 | 1.0 | .... | .... | 5.7 | 1.0 | .... | + | .... |
| Leucin | 20.48 | 18.70 | 10.6 | 10.5 | 15.0 | 11.8 | 29.9 | 18.3 | 21.4 | 2.1 | 1.5 | 22.2 |
| Glutamic acid | 7.7 | 8.5 | 6.0 | 11.0 | 3.6 | 0.5 | 1.73 | 3.0 | 0.8 | 14.0 | 0 | 3.8 |
| Aspartic acid | 3.12 | 2.54 | 4.5 | 1.2 | 2.0 | 0 | 4.43 | 2.5 | .... | 0.56 | + | .... |
| Serin | 0.6 | .... | .... | 0.23 | 0.8 | .... | 0.6 | 0.7 | .... | 0.4 | 1.6 | .... |
| Cystin | 2.53 | 0.7 | .... | 0.065 | .... | .... | 0.31 | .... | .... | .... | .... | .... |
| Lysin | .... | .... | + | 5.80 | 4.0 | 6.9 | 4.28 | .... | + | 5–6.0 | + | 11.6 |
| Arginin | .... | .... | + | 4.84 | 30.0 | 15.5 | 5.42 | .... | 0.3 | 9.3 | 4.0 | 13.9 |
| Phenylalanin | 3.08 | 3.84 | 1.5 | 3.5 | 2.5 | 2.2 | 4.24 | 3.0 | 3.9 | 0.4 | 1.5 | .... |
| Tyrosin | 2.1 | 2.5 | 1.7 | 4.5 | 3.5 | 5.2 | 1.5 | 4.6 | 0.34 | 0 | 10.5 | 4.0 |
| Prolin | 1.04 | 2.76 | 1.9 | 3.1 | 3.6 | 1.5 | 2.34 | 3.6 | 1.7 | 5.2 | + | 3.1 |
| Oxy-Prolin | .... | .... | .... | 0.25 | .... | .... | 1.04 | .... | .... | 3.0 | .... | .... |
| Tryptophan | + | + | .... | 1.5 | .... | .... | + | .... | 0 | 0 | + | .... |
| Histidin | .... | .... | + | 2.59 | + | 1.5 | 10.96 | .... | 0.3 | 0.4 | + | 0 |
| Glucosamin | .... | + | .... | .... | .... | .... | .... | .... | .... | 0 | .... | .... |
| Ammonia | 1.2 | 1.75 | 1.6 | 1.8 | + | 1.66 | 0.93 | .... | .... | 0.43 | .... | .... |

## *2. The Polypeptids*

These consist of shorter and longer chains of amino acids; thus, a chain consisting of two acids is called a *dipeptid* (*e. g.*, glycyl-l-tyrosin), one of three acids a *tripeptid* (*e. g.*, l-leucyl-glycyl-d-alanin); *tetrapeptids, pentapeptids, hexapeptids, octapeptids, decapeptids, tetradecapeptids* and *octadecapeptids* are known. Some of these have been isolated from mixtures obtained by partially hydrolyzing proteins; others have been made synthetically (Emil Fischer).

## *3. The Peptones and the Albumoses*

Some of the polypeptids resemble "peptones" closely, and some, especially tripeptids and pentapeptids containing l-tyrosin, resemble "albumoses" extraordinarily. The probability is that albumoses do not have very large molecules, as was formerly supposed, but that the so-called albumose-reactions depend upon the kinds of amino acids present in chains at various stages of the degradation of proteins. It has been suggested that the term "albumose" be dropped altogether and that, instead, the term "peptones not precipitable by ammonium sulphate" be used.

Though, in reality, peptones, albumoses, and proteins are chains of amino acids (*i. e.*, polypeptids), the term polypeptid is, at present, arbitrarily reserved for the chains that have lost their peptone-character, i. e., those that no longer yield a biuret-reaction.

### iv. The Course of Protein Metabolism

The following scheme, constructed by Taylor, illustrates well the main facts of protein metabolism, including exogenous protein.

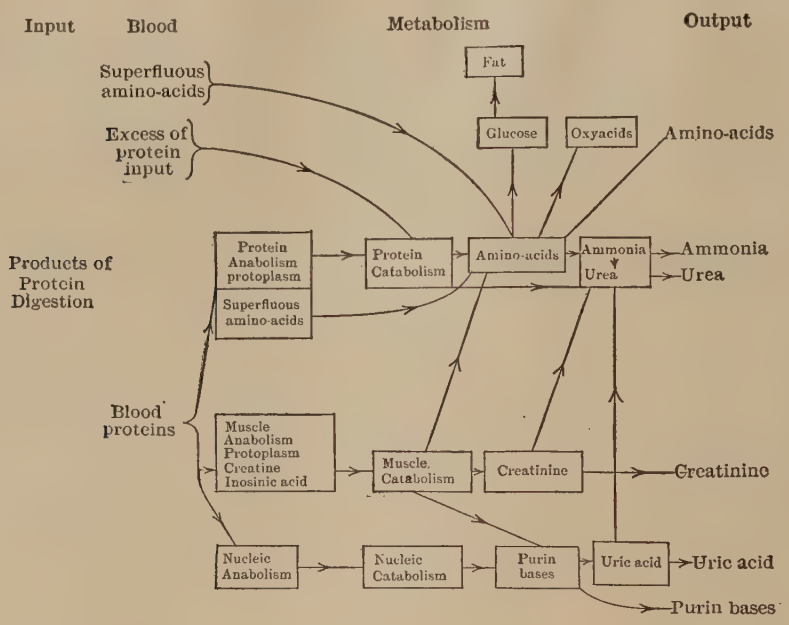



Fig. 632.—Course of Protein Metabolism. (After A. E. Taylor, in his "Digestion and Metabolism," published by Lea & Febiger, Philadelphia.)

### v. General Chemical Properties of the Proteins

#### *1. Proteins as Colloids*

They behave physically as **hydrophile colloids**, occurring as *sols* in the body fluids, but go easily from the **sol-state** to the **gel-state**, sometimes reversibly (precipitation by neutral salts), sometimes irreversibly, when they are "denatured" (precipitation by salts of the heavy metals like $HgCl_2$ $CuSO_4$, $Pb(C_2H_3O_2)$; coagulation by heat).

The *molecular weights* of the principal proteins are not exactly known, but they must be very large. Thus, it is estimated that the molecular weight of serum-albumin is 5,100, that of oxyhemoglobin 14,800.

#### *2. Proteins as Electrolytes*

The proteins have both acid and basic qualities and can form *salts* with both acids and bases; they are **amphoteric electrolytes**, of the general formula H. alb. OH, and can, on *dissociation*, yield either H-ions or OH-ions; they can thus play an important part in temporarily neutralizing, either an excess of acid, or an

excess of alkali (maintenance of equilibrium between acids and bases in the organism).

The proteins are *optically active;* in aqueous solutions, they are *laevorotary.*

### 3. *Color Reactions for Proteins*

There are a great many; the most important are (1) the biuret reaction, (2) the xanthoprotein reaction, (3) Millon's reaction, (4) the PbS reaction, (5) the reaction of Molisch, (6) the Hopkins and Cole reaction, and (7) the reaction of Neubauer and Rohde.

1. **The Biuret Reaction.**—Make the solution alkaline with KOH; add 1-3 drops dilute solution of $CuSO_4$. If proteins, albumoses, or peptones be present, a *bluish-violet color* (native proteins), or a *red color* (histons; peptones) will appear. Avoid excess of $CuSO_4$.

The biuret reaction depends upon the presence of *pairs of groups* of the character $-CONH_2$, $-CSNH_2$, $-C(NH)_2$, or $-CH_2NH_2$ (Schiff).

2. **The Xanthoprotein Reaction.**—On warming with strong $HNO_3$, solutions or precipitates of protein turn yellow; on adding excess of NaOH, the color turns red-brown. This is due to the *nitration of benzene-groups or of indol-groups.* The yellow color of the skin touched with nitric acid is an example.

3. **Millon's Reaction.**—Boil the solution containing protein with Millon's reagent, a solution of Hg in $HNO_3$ (containing some $HNO_2$), or with Nasse's reagent (aqueous solution of acetate of mercury, to which, just before use, a few drops of 1 per cent solution of $NaNO_2$ are added). A precipitate forms, which, on warming, turns intensely red. The reaction depends on the presence of the *oxyphenyl-group* in tyrosin; hence, proteins like gelatin, that do not contain tyrosin, fail to yield Millon's reaction.

4. **The PbS Reaction.**—Boil the solution containing protein with NaOH and a lead salt; a black precipitate of PbS is formed. This reaction depends upon the presence of *cystin.*

5. **The Reaction of Molisch.**—To 1 c.c. of the solution containing protein, add two drops of a 20 per cent solution of *a*-naphthol, and then 1-2 volumes of concentrated $H_2SO_4$; a ruby red, or a violet color appears, which, on adding alcohol, ether, or NaOH, turns yellow. The reaction depends upon the carbohydrate-group (*glucosamin*) of the protein molecule; hence, proteins like casein, devoid of carbohydrate, do not give it.

6. **The Reaction of Hopkins and Cole.**—To the solution containing the protein, add some glyoxylic acid ($COOH-COH$) (obtained by adding sodium amalgam to a strong solution of oxalic acid, and after gas ceases to be given off, filtering), and then some concentrated $H_2SO_4$; a blue violet color appears. The reaction depends upon the presence of *tryptophan.*

(The *reaction of Liebermann,* and the *reaction of Adamkiewicz,* are due to contaminations of the reagents with glyoxylic acid!)

7. **The Reaction of Neubauer and Rohde.**—To the solution (or suspension) of protein, add 5-10 drops of a 5 per cent solution of p-dimethylaminobenzaldehyde in 10 per cent $H_2SO_4$; while shaking the tube, run in some concentrated $H_2SO_4$; a reddish-violet color appears, changing to dark violet. The reaction seems to depend upon the presence of *tryptophan.*

### 4. *Precipitation-Reactions for Proteins*

The most important are (1) the *salt*-precipitations, (2) precipitation with *alcohol,* (3) coagulation by *heat* in feebly acid solutions, (4) precipitation by

*strong acids*, e. g., $HNO_3$, and (5) precipitation by the so-called "*alkaloid-reagents*," *e. g.*, phosphotungstic acid, trichloracetic acid, picric acid, sulphosalicylic acid, and potassium ferrocyanid with acetic acid.

### (c) *The Constant Need of Protein by the Body*

Life cannot be maintained long without the addition of protein to the diet. A man fed only on fat, sugar and starch will die.

Moreover, in foodstuffs, there are **different kinds of protein,** and the variety of protein ingested is by no means unimportant. Thus, the proteins of milk, meat, fish, gelatine, bread and vegetables vary considerably in their constitution. During digestion, as we have seen, all the proteins are broken up into their constituent amino acids, of which, as we have also seen, there are many varieties. These amino acids can be combined in different ways so as to form different kinds of proteins, just as the letters of the alphabet can be combined in different ways to form different words.

To quote from Lusk: "Suppose the word *albumin* were broken up by digestion into the letters *a, b, i, l, m, n, u,* then if these letters were absorbed they could be reconstructed into *albumin* again. Assume the same for the word *globulin.* Now if both *albumin* and *globulin* were to be formed from a common word, one would have to ingest a hypothetical substance called *amglobulin,* convertible into *globulin* if the letters *a, m,* are abandoned to their fate, or into *albumin* on similarly exorcising the letters *l, g.* Carrying the analogy still further, it is evident that if the letter *b* were not in the word *amglobulin,* neither *albumin* nor *globulin* could possibly be produced."

### (d) *Superior and Inferior Proteins in Foods*

The **physiological value of the different proteins** varies, therefore, with their content in elementary amino acids, and a very good idea of the content of some of the more important proteins can be gained from the table given above in the résumé of the physiological chemistry of the proteins.

Thus, **casein,** contained in milk and cheese, contains practically all of the amino acids that enter into the formation of the different kinds of protein of the body cells. Broken up during digestion into its constituent building stones (amino acids), the latter can be rearranged in the body to form the proteins required for the structure of the cells in the different organs. It has been shown that a child can transform as much as 40 per cent of the protein in its food (largely casein of milk) into new structural machinery, "the architecture of which depends upon a regrouping of individual units formerly in the protein of milk."

Among the **superior proteins,** that is, those especially valuable for human food, because they contain the amino acid units that when rearranged can form the proteins of the human body, are those of *milk, meat,*

*eggs* and *fish*. Among the **inferior proteins** are those of *bread, beans,* and *Indian corn*. The proteins of *rice* and *potato* occupy an intermediate position.

The relative physiological value of proteins of different origin is well shown by the experiments of Thomas, according to which the following minimal amounts of protein were required to protect the body protein from loss:

| | |
|---|---|
| Meat protein | 30 grams |
| Milk protein | 31 grams |
| Rice protein | 34 grams |
| Potato protein | 38 grams |
| Bean protein | 54 grams |
| Bread protein | 76 grams |
| Indian corn protein | 102 grams |

Lusk suggests that facts such as these should make it possible for us to *classify proteins* in groups according to their physiological value. Just as milk is sold in our large cities as of three grades, A, B, and C, in like manner the proteins of food stuffs could be labelled A, B, and C, according to their physiological value, and in another group, D, might be placed *gelatine* and certain other proteins that are incapable, in themselves, of replacing body protein.

Most important, in this connection, are the **researches of Osborne and Mendel** of New Haven. Osborne has shown that in *wheat* two important proteins are present in approximately equal amounts; namely, *wheat glutenin* and *wheat gliadin,* the former having a content in amino acids similar to that of casein, the latter being very different, since it contains no *lysin* and has an excess of glutamic acid (37 per cent), contrasted with the lower glutamic acid content (10 per cent) of the protein of milk and muscle. Feeding experiments with animals revealed remarkable differences according as glutenin or gliadin were used. In the one instance, growth was satisfactorily maintained; in the other, the animals were dwarfed, though if the missing amino acid unit, lysin, were added to the gliadin diet, the animals began to grow. In *Indian corn,* there are also two important proteins, *glutenin* and *zein*. The former is a superior protein, the latter a protein of inferior type, since, like gelatine, it contains no *tryptophan*. Animals fed on zein failed to grow, but if the missing tryptophan were added to the zein diet, life was much prolonged, and, in some instances, weight was maintained.

Phaseolin, a protein of the *kidney bean,* is much like zein. Animals fed upon it failed to maintain their body weight owing to the lack of some necessary amino acid in its constitution.

**Casein** is one of the most valuable of all the proteins. Osborne and Mendel have shown that it can cause normal growth and that all the proteins of the body, even the more complex ones (hemoglobin, elastin, collagen, keratin, etc.) can be made from it. *Glycocoll,* it is true, is absent from casein, but the animal body has the power to make glycocoll artificially from casein. The body does not, however, possess the power to build tryptophan or lysin artificially, and this is probably the reason why gelatin, gliadin and zein cannot supply the building stones from which there can be formed the body protein necessary for the repair of the body machinery.

It is true that if all the proteins present in bread and in corn be considered, these grains will be found to contain all the amino acids necessary for the building of body protein, and if enough bread or corn be eaten, human life can be maintained on such a vegetable diet. But, on such a diet a very extravagant use of proteins is involved, since the proportions of amino acids are such that a great many of them cannot be utilized for the synthesis of body proteins. Animals exist on plant proteins, it is true, reconstructing the constituent amino acids into beef, mutton and pork proteins, and oxidizing and eliminating the excess of the chemical units that are unnecessary for the structure of animal cells. Human beings, through eating meat and milk, obtain proteins much better suited for the manufacture of their own body proteins than the less closely related proteins of the vegetable kingdom.

It is, however, not a serious matter if the healthy body takes (1) a certain amount of protein of inferior grade, or (2) proteins of superior type in excess of the bare requirement necessary to repair the tissues of the body; for the amino acids that cannot be utilized in the building of body protein, or even an excess of those that can be so used, will be used as fuel and burned, just as fat and carbohydrates are burned. The amino acids undergo deaminization with formation of ammonia and urea, and their nitrogen-free residues easily undergo oxidation to carbon dioxid and water. Excess of protein in the diet throws extra work on the kidneys, which must eliminate the urea formed if it is not to be retained and cause intoxication.

It is probable that the proteins of serum (*serum-albumin* and *serum globulin*) are again broken up as required by the single cells of the different organs of the body. The studies of J. J. Abel by the method of dialysis, with utilization of the so-called artificial kidney or *vividiffusion,* have shown, however, that free amino acids are always present in the blood, and that by prolonged dialysis large quantities of these can be removed from the circulating blood. It seems likely, then, that the individual body cells can abstract from the blood, at need, the particular building stones required for the architecture of their special proteins. The careful studies of Van Slyke and his associates are throwing light upon the distribution of amino acids in the several organs of the body.

### (e) *The Physiological Decomposition of Protein in the Body Metabolism*

Certain facts regarding the disintegration of protein in the body should be kept in mind. In the first place, the metabolism of protein is more or less independent of the protein intake. During *starvation,* protein is continuously metabolized. In non-fasting persons, the more protein ingested, the more the body metabolizes, though, gradually, the

protein metabolism adapts itself to the protein intake, so that *protein equilibrium* exists, or, in other words, the body exactly maintains the amount of its protein, neither losing nor gaining protein.

Fats, carbohydrates and alcohol, if ingested along with protein, diminish somewhat the amount of protein metabolized; in other words, they are **"sparers" of protein.**

The **end-products of protein metabolism** include *urea, ammonia, carbon dioxid* and *water.*

In **intermediary metabolism** of protein, *polypeptids, amino acids* and the *nitrogen-free residues* of deaminized amino acids, are the important substances.

Since **nitrogen** is present in proteins in fairly constant amount (16 per cent), it is customary to measure total protein metabolism by the *nitrogen of the intake,* on the one hand, and the *nitrogen of the output* (in the urine and feces), on the other, since by multiplying the amount of nitrogen by $\frac{100}{16} = 6.25$, the corresponding amount of protein is obtained.

### *(f)* *Protein Balance; Nitrogen Balance*

In protein metabolism we may have (1) a condition in which protein is neither added nor lost (*protein equilibrium; nitrogen equilibrium*), (2) a condition in which the amount of protein in the body is increased (*protein gain; positive nitrogen balance*), or (3) a condition in which the protein of the body is diminished (*protein loss; negative nitrogen balance*).

If a man be *starved* completely, the nitrogen excretion in the urine will become constant after a few days, and will amount to about 0.1-0.3 g. of N per kilo of body weight. If the man be *not starved,* but be fed on carbohydrate and fat, without any protein, the nitrogen loss will be somewhat diminished. *To maintain nitrogen equilibrium,* protein must be added to the carbohydrate and fat, and in somewhat larger amounts than the amount that corresponds to the nitrogen excretion during complete starvation; the protein of the intake must be accompanied by sufficient carbohydrate and fat to *cover the caloric needs* of the body. Finally, as we have seen, the food intake should include *superior proteins,* that is to say, proteins that contain, and in suitable proportions, the amino acids required for the constitution of the body proteins.

The **minimal protein intake** that will maintain nitrogen equilibrium has been carefully studied by Chittenden. It varies in quantity under different circumstances (30-80 grams protein per day).

A **protein-gain** (with *positive* nitrogen-balance) is difficult to produce, except under certain conditions. Even when large amounts of protein of superior type are ingested, the body strives for protein equilibrium, and proteins ingested in excess of the amount necessary for this are oxidized and eliminated. However, during *growth,* in *convalescence* after

severe disease, or in *states of under-nutrition,* the protein-gain may be quite marked on a liberal diet. A less pronounced protein-gain can be observed on liberal feeding if much *muscular exercise* be taken, or on removal to a *mountain climate.*

**A protein-loss** (with *negative* nitrogen balance) occurs in all states of under-nutrition (*starvation, wasting diseases, fever, hyperthyroidism,* etc.).

On *removal of exudates* (repeated tapping of a pleural effusion or of an ascites), there is an outspoken protein-loss. If such exudates undergo absorption, the proteins are quickly oxidized and eliminated (*epicritical excretion of nitrogen* in pneumonia).

In fever, in cachexias, and in certain intoxications, there may be a marked destruction of protein with outspoken nitrogen loss and negative nitrogen balance. This is the so-called *toxic destruction of protein.*

In the states referred to above, we have considered only conditions in which the kidneys function normally. But the N-balance may be disturbed, even when the actual nitrogen metabolism is unchanged, owing to **alterations in excretion** of nitrogenous bodies. Thus, on the one hand, after *abundant water-drinking,* larger amounts of urea than normal may be washed out of the body, for a brief period. On the other hand, in the nephropathies, where *renal insufficiency* exists, the nitrogenous end-products of protein metabolism may not be excreted as rapidly as is normal, in which event they are retained in the blood and accumulate in the body. Other excretory organs may compensate, more or less, for the renal insufficiency; thus, more urea than normal may be excreted through the sweat and through the feces. But, sooner or later, the retention in the blood becomes marked and along with other retained substances causes outspoken intoxication **(uremia).**

### (*g*) *Synthesis of Pathological Proteins in the Body*

In pathological states, abnormal proteins may arise within the body. Thus, in amyloid degeneration of the organs, the **amyloid protein** is formed. In tumors of the bone-marrow, and in some cases of leukemia (Boggs and Guthrie), the **Bence-Jones protein** is formed in large amounts, and is excreted as such in the urine.

### (*h*) *Excretion of Non-metabolized Amino Acids in Pathological States*

When large amounts of protein undergo sudden disintegration in the body, as in **acute yellow atrophy** of the liver, or in **phosphorus poisoning,** products of the intermediary metabolism of protein, such as the amino acids, may be excreted in the urine as such, without being metabolized.

Leucin, tyrosin, glycocoll, and phenylalanin, may, in such circumstances, appear in the urine (Abderhalden and Barker).

Again, in certain *congenital disorders of metabolism,* faults of intermediary metabolism are discernible; thus, in **alcaptonuria** *homogentisic acid* is excreted in the urine; in **cystinuria** the sulphur-holding amino, acid *cystin* is excreted in the urine (See Amino Acid Diatheses).

### (*i*) *The Specific Dynamic Action of Protein*

Among the many remarkable properties of protein, one more must be especially referred to. More than any other foodstuff, protein has the power to *increase the production of heat* in the body.

People who live in the tropics tend to eat but little protein. The Eskimos, who live in the Arctic region, eat enormous quantities of protein. People who live on a low protein diet often suffer intensely from the cold. The best fortification against cold on a severe winter day is a large meal of beefsteak or of roast beef.

The heat production of an animal may be doubled by *excessive meat-feeding,* and experiments have shown that the *feeding of single amino acids,* such as glycocoll, will stimulate heat production. Even in diabetes, when the glycocoll ingested is converted into sugar, and does not undergo oxidation, it still, when fed, causes increased heat production—a very remarkable fact. These amino acids seem to act, in such circumstances, as *chemical stimuli,* rather than by virtue of their energy-content. This **specific dynamic action of protein,** as Rubner calls it, holds for all kinds of protein, for those of inferior, as well as for those of superior, type; in other words, as Lusk puts it, "to obtain the warming effect, it is not necessary to purchase beef, a relatively costly article of diet."

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## 3. The Metabolism of Nucleins and Purins

### (*a*) *Introduction*

The nuclei of cells in foodstuffs and in the animal body are very different chemically from the protoplasm of the cells. They contain nucleins, which are exceedingly complex chemical substances. These nucleins are insoluble acids that form soluble sodium salts. They yield some of the color reactions of protein (*q. v.*), but differ from ordinary proteins in the phosphoric acid that they contain, and especially, in the resistance that they offer to the solvent action of artificial, and natural, gastric juice.

Miescher's studies showed that the *nucleins of the heads of spermatozoa* consist almost exclusively of a salt, composed of an inorganic base (rich in nitrogen), known as *protamin,* and of an organic acid (containing

phosphorus) known as *nucleic acid.* Kossel demonstrated the presence of alloxuric bases, afterwards known as purin bases, in nucleic acid, these acids on hydrolysis yielding two aminopurins (guanin and adenin), which on oxidation yield the two oxypurins, xanthin and hypoxanthin. These oxypurins, when further oxidized, yield uric acid, a trioxypurin.

The conviction has become general that *all nucleins consist of combinations of nucleic acid with protein;* in other words, that nuclein is a salt of nucleic acid. The study of nuclein metabolism therefore resolves itself into (1) the study of the metabolism of proteins (see above), and (2) the study of the metabolism of nucleic acid (see below).

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## (*b*) *The Nucleic Acids and the Nucleotides*

### i. Nucleic Acid in Animals and Plants

It turns out, as a result of recent studies, that there are two great types of nucleic acid, one peculiar to the nuclei of animals (*animal nucleic acid*) and one peculiar to the nuclei of plants (*plant nucleic acid*).

The **animal nucleic acid** that has been best studied is that derived from the nuclei of the cells of the thymus gland (*thymus nucleic acid*), and it seems likely that the nucleic acids of the nuclei of other cells in the human and animal body are identical, or nearly identical, with this thymus nucleic acid.

The **plant nucleic acid** that has been best studied is that derived from the nuclei of the cells of yeast (*yeast nucleic acid*), and it seems likely that the nucleic acids of the nuclei of other cells in the vegetable kingdom are identical, or nearly identical, with this yeast nucleic acid.

Studies of the *cleavage* of these nucleic acids make it seem certain that each consists of a chain of four simpler bodies known as **nucleotides**; in other words, the nucleic acids are *tetranucleotides.*

The **tetranucleotides** can be cleft into two **dinucleotides,** each of which can in turn be cleft into two **mononucleotides.**

### ii. The Mononucleotides

Now each *mononucleotide* is itself a chain consisting of three links, of which the middle link is a carbohydrate group, one end-link is a phosphoric acid group, and the other end-link is a base:

**Phosphoric acid—Carbohydrate—Base.**

The *phosphoric acid* group, which forms one end-link, seems to be the same in all mononucleotides, whether derived from animal nucleic acid or from plant nucleic acid.

The *carbohydrate* group, which forms the middle link of the nucleotide chain, has been found in plant nucleic acid to be a pentose, namely d-ribose. In the mononucleotides of animal nucleic acid, the carbohydrate link is not a pentose but a hexose; its exact nature is not understood, but it is known to yield levulinic acid as a secondary product.

The *base,* forming the link at the other end of the mononucleotide chain, is different for each of the four nucleotides of which the tetranucleotide, plant nucleic acid, is made up. In two of these mononucleotides, it is a purin base (guanin in one, adenin in the other); whereas in the other two mononucleotides of plant nucleic acid, it is a pyrimidin base (uracil in one, cytosin in the other).

The four mononucleotides of *plant nucleic acid* are then:

A. Purin Base Mononucleotides.

1. *Guanin-mononucleotide* (= Phosphoric acid—d-ribose — guanin).
2. *Adenin-mononucleotide* (= Phosphoric acid—d-ribose—adenin).

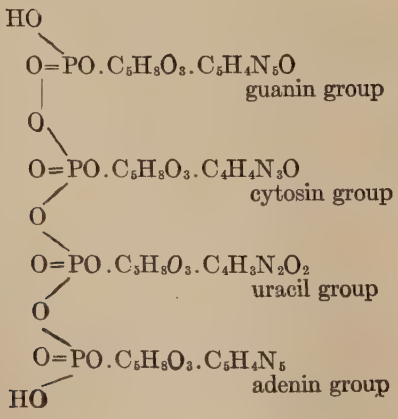
B. Pyrimidin Base Mononucleotides.

3. *Uracil-mononucleotide* (= Phosphoric acid — d-ribose — uracil).
4. *Cytosin-mononucleotide* (= Phosphoric acid—d-ribose—cytosin).

In *animal nucleic acid,* there are also two purin bases (guanin and adenin) and two pyrimidin bases (thymin and cytosin), a different base for each of the four mononucleotides of which animal nucleic acid is composed. It will be observed that the two purin bases are identical for the two types of nucleic acid; of the pyrimidin bases one (cytosin) is present in both nucleic acids, but plant nucleic acid contains uracil (and not thymin), while animal nucleic acid contains thymin (and not uracil).

### iii. Structure of Plant Nucleic Acid

The formula of plant nucleic acid may, therefore, be conceived of as represented by the formula:

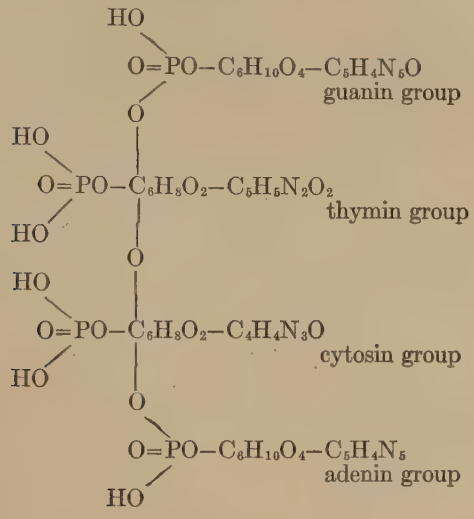


Its composition, as a tetranucleotide chain composed of four constituent mononucleotides united in the form of a polyphosphoric acid, will be obvious from a view of the above formula.

I have placed the guanin-mononucleotide next in the chain to the cytosin-mononucleotide, since Walter Jones has been lucky enough to split yeast nucleic acid into two dinucleotides, one of which yielded guanin and cytosin, but neither adenin nor uracil, and the other yielded adenin and uracil but no cytosin, and only a trace of guanin (probably a slight impurity).

### iv. The Structure of Animal Nucleic Acid

The formula of animal nucleic acid may, in turn, be conceived of, according to Levene and Jacobs, as represented by the formula:




### v. Hydrolysis of Nucleic Acids

The products of hydrolysis of the two nucleic acids actually found, are as follows:

Hydrolytic Products of Nucleic Acid

| Of Plant Origin | Of Animal Origin |
|---|---|
| Phosphoric acid | Phosphoric acid |
| Guanin | Guanin |
| Adenin | Adenin |
| Cytosin | Cytosin |
| Uracil | Thymin |
| Pentose | Levulinic acid |

### vi. Manufacture of Nucleic Acid by the Human Body

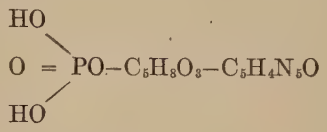
The human body is capable of forming its own nucleic acids and cell nuclei on a purin free diet; thus, the new-born infant lives for many months on a milk diet, which is purin free. Patients who suffer from gout often live for long periods on a diet that is practically purin free.

The disturbances of purin metabolism observable in gout, in leukemia, and in certain other conditions, are referred to in the sections dealing with special diseases of metabolism (Part XIII, Section ii).

### vii. Extranuclear Nucleotides

Aside from the nucleotides that are constituents of the nucleic acids that occur in the nuclei of the cells of the body and in the nuclei of cells (animal and vegetable) of the food, certain extranuclear nucleotides are now known to exist in the human and animal body. I refer to (1) *guanylic acid* and (2) *inosinic acid.*

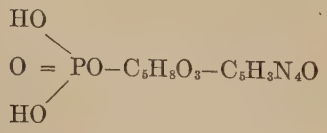
**Guanylic acid** is an extranuclear substance present in considerable quantity in the pancreas and other glands. It was at first supposed to be a nucleoprotein (betanucleoprotein of Hammarsten), but the evidence now is in favor of an extranuclear origin. It has been shown to have the following structure:



It will be seen at once that this is identical with the guanin mononucleotide of nucleic acid. Like the latter body, it yields, on hydrolysis:

Phosphoric acid + d-ribose + guanin.

**Inosinic acid** is an extranuclear substance present in considerable quantity in muscle. It has been shown to have the following structure:



It will be seen at once that this is the structure of a pentose-nucleotide, closely resembling the adenin-mononucleotide of plant nucleic acid, but differing from it in that the adrenin group (an aminopurin) is replaced by its deaminized product hypoxanthin (an oxypurin). Thus inosinic acid, on hydrolysis, yields:

Phosphoric acid + d-ribose + hypoxanthin.

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### (c) *Nucleosides*

Having studied the general structure of the mononucleotides we are now able to understand the structure of nucleosides. A **nucleoside** is simply a mononucleotide chain, deprived of one of its end-links. Thus a mononucleotide has the structure:

Phosphoric acid — carbohydrate — base.

This may lose either the phosphoric acid end-link and so become a "carbohydrate-base nucleoside," or the base end-link and become a "phosphoric-acid-carbohydrate nucleoside."

Take, for example, the *guanin-mononucleotide* of plant-nucleic acid; either it may lose the end-link phosphoric acid and give rise to d-ribose-guanin (known as the nucleoside "guanosin"), or it may lose the end-link guanin and give rise to the nucleoside "d-ribose-phosphoric acid." Thus, on hydrolysis of guanin-mononucleotide, the molecule may split at (1) or at (2):

$$H_2PO_4-C_5H_8O_3-C_5H_4N_5O + H_2O$$

(1) (2)

(1) $= H_3PO_4 + C_5H_9O_4 - C_5H_4N_5O$

= Phosphoric acid + guanosin

or (2) $= H_2PO_4-C_5H_9O_3 + C_5H_5N_5O$

= d-ribose–phosphoric acid + guanin

Thus from the four mononucleotides of plant nucleic acid, by splitting off the phosphoric acid end-link, four nucleosides are formed. They are:

A. Aminopurin nucleosides:

1. *Guanosin* (=d-ribose – guanin)
2. *Adenosin* (=d-ribose – adenin).

B. Aminopyrimidin nucleosides:

3. *Cytidin* (=d-ribose – cytosin)
4. *Uridin* (=d-ribose – uracil).

From the four mononucleotides of animal nucleic acid, four glucosides (*hexose-nucleosides*) should be obtainable (hexose-guanin, hexose-adenin, hexose-cytosin, and hexose-thymin).

It is interesting that the extranuclear mononucleotides, *guanylic acid* and *inosinic acid*, similarly yield nucleosides, in the one instance *guanosin*, in the other, *inosin* (= hypoxanthosin).

The aminopurin nucleosides, *guanosin* and *adenosin*, are easily converted into the corresponding oxypurin nucleosides, *xanthosin* and *inosin*, and the aminopyrimidin nucleoside, *cytidin*, can be converted into the corresponding oxypyrim-

idin nucleoside, *uridin.* The *purin nucleosides* are easily broken up into carbohydrate and the corresponding purin. Thus *guanosin* yields *guanin; adenosin* yields *adenin;* and *inosin* yields *hypoxanthin.* The *pyrimidin nucleosides* are very resistant to hydrolysis.

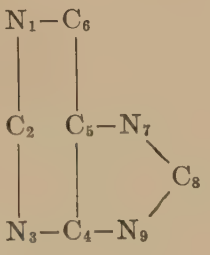
### (*d*) *The Purins*

#### i. Structure of the Purins

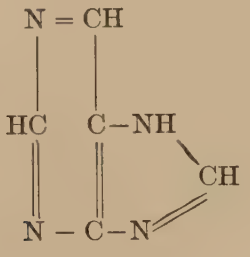
We have seen that certain purin bodies enter into the formation of nucleic acid and its constituent nucleotides and nucleosides.

*Guanin, hypoxanthin, xanthin,* and *uric acid* have long been known in metabolic studies; a fifth body, *adenin,* was discovered by Kossel in 1886. These five substances must be looked upon as chemical derivatives of a mother-substance known as **purin,** hypothetically formulated by Emil Fischer in 1898, and afterwards synthetically prepared by him. The following formulae explain themselves:

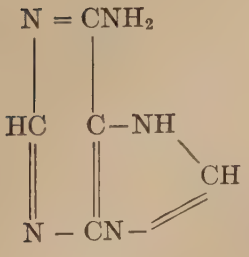
**Purin Nucleus**
(Atoms numbered according to E. Fischer)



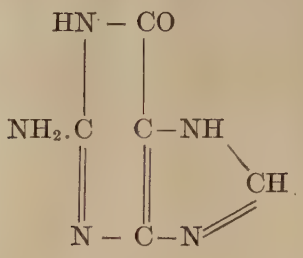

**Purin** ($C_5H_4N_4$)



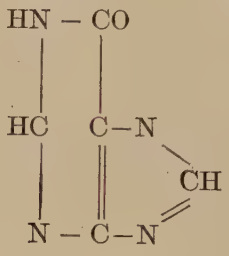

**Adenin** ($C_5H_5N_5$) = 6-aminopurin:



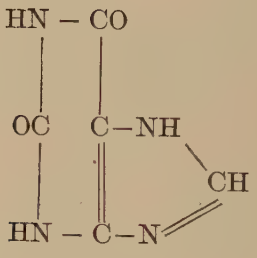
**Guanin** ($C_5H_5N_5O$) = 2-amino-6-oxypurin:



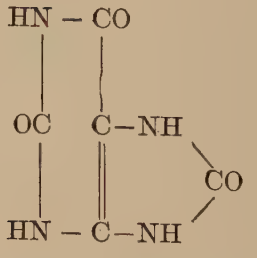

**Hypoxanthin** ($C_5H_4N_4O$) = 6-oxypurin:



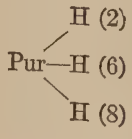

**Xanthin** ($C_5H_4N_4O_2$) = 2-6-dioxypurin:



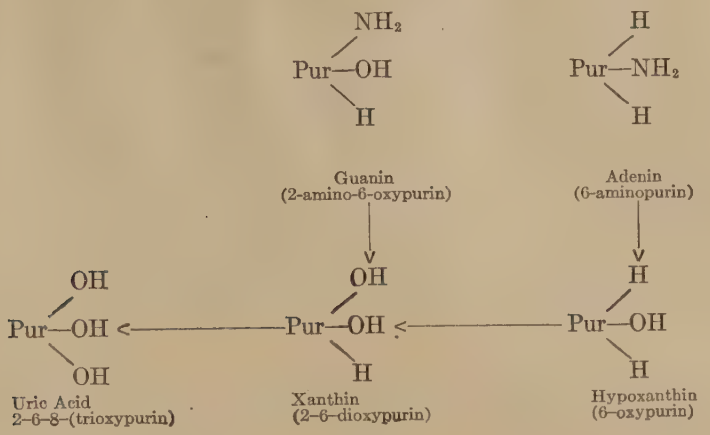

**Uric Acid** ($C_5H_4N_4O_2$) = 2-6-8-trioxypurin:




A somewhat similar method of representing these bodies is as follows. For the purin nucleus with its three replaceable hydrogen atoms, we may write the abbreviated expression:



Then the relation to one another of the five purin compounds that interest us especially in human metabolism can be seen from the following formulae:

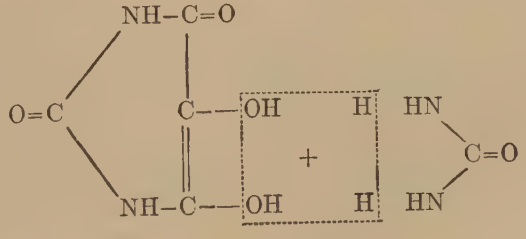



### ii. Syntheses of Purin Bases

The four different purin bases (guanin, adenin, xanthin, and hypoxanthin) have been made artificially from uric acid by Emil Fischer. Chemists have shown also that the *aminopurins* can be converted, chemically, into the *oxypurins* by the action of nitrous acid. *Uric acid* can be formed from all four of the bases. Thus, *guanin* and *adenin* may undergo deaminization to form the oxypurins *xanthin* and *hypoxanthin,* which, in turn, can be oxidized to *uric acid.* Or, the oxidation may precede the deaminization, in which event the end-product is the same but the intermediate products are different.

### iii. Synthesis of Uric Acid

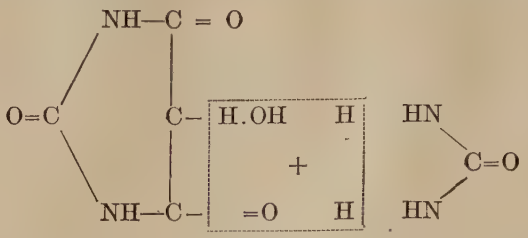
Uric acid can be made synthetically, in the test tube, from urea and 4-5-dioxy-uracil:




In birds, uric acid is formed synthetically in large amounts in normal metabolism (Minkowski, v. Mach). This occurs in the liver, from ammonia and lactic acid.

In surviving organs of mammals, or in organ pastes (calves' liver, ox liver, dog's liver) in the presence of $CO_2$ and of blood, uric acid may be synthesized. It has

been suggested that in this synthesis, dialuric acid and urea are united to form uric acid (Ascoli and Izar):

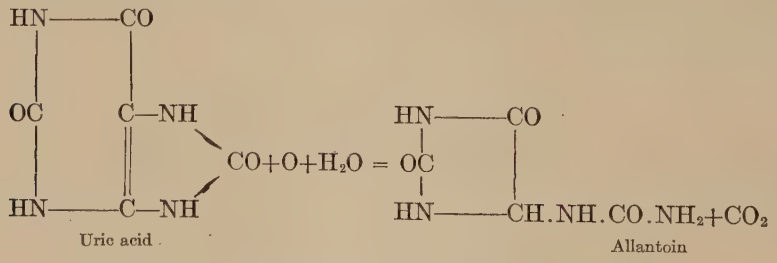



The evidence is strongly against the formation of any considerable amount of uric acid synthetically in man, though the purin bases are doubtless synthesized to a large extent (certainly in sucklings, and in persons who live for long periods on a purin-free diet).

### iv. Oxidation Products and other Transformations of Uric Acid

On treatment with water and oxygen, in the presence of suitable catalyzers, uric acid can be converted (1) into glycocoll, ammonia and carbon dioxid, (2) into urea and alloxan, (3) into oxalic acid, ammonia and carbon dioxid, or (4) into allantoin and carbon dioxid.

As long ago as 1860, Stockvis showed that uric acid is destroyed in the body of animals, a fact rediscovered by Wiener (1902-3). As far as is known, the fourth of the reactions above mentioned is the only one that occurs in the animal body. Indeed, in many animals (ox, horse, cat, dog, rabbit), **allantoin** (and not the uric acid from which it is derived) must be looked upon as the principal end-product of purin-metabolism. In these animals, the catalyzer is a ferment, known as the *uricolytic* ferment, or **uricase.** The reaction is as follows:




It will be observed that allantoin is the diureid of glyoxylic acid.

This allantoin-formation from uric acid does not occur in human tissues (Wiechowski), probably owing to the fact that no uricase exists in the human organs that have been tested (Batelli and Stern; Winternitz and Jones; Miller and Jones). For the present, then, we must look upon uric acid as the main end-product of purin metabolism in man, since in him no mechanism for the oxidation of uric acid to allantoin exists.

### v. The Methyl Purins

The *methyl purins* derived from tea, coffee, cocoa, and certain medicines (coca cola, caffein, diuretin, theocin) include (1) *caffein,* (2) *theobromin,* and (3) *theophyllin.*

*Caffein* is 1-3-7-trimethylxanthin; *theobromin* is 3-7-dimethylxanthin; and *theophyllin* is 1-3-dimethylxanthin.

It seems that *uric acid* is not formed from these methyl purins when they are ingested.

They undergo certain changes in the animal body before excretion in the urine, the changes varying somewhat with the species of animal. In *man,* ingested *caffein* is excreted as 1-7-dimethylxanthin (or paraxanthin); *theobromin* is excreted as 7-methylxanthin (heteroxanthin); and *theophyllin* is excreted as 1-methylxanthin.

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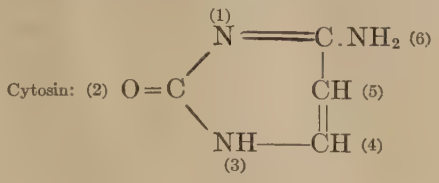
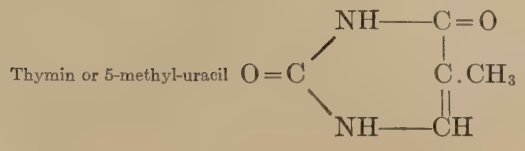
### (e) *The Pyrimidins*

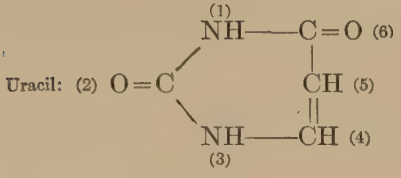
Three different **pyrimidin bodies** are of interest in connection with the metabolism of the nucleic acids. They are (1) *cytosin,* (2) *thymin,* and (3) *uracil.*

**Cytosin** is met with among the disintegration-products of both animal and plant nucleic acid; **thymin** is derived from animal nucleic acid only,

and **uracil** from plant nucleic acid only. The structure of these three bodies will be clear from the accompanying formulae:




It will be noticed that, in cytosin, the amino-group is in position 6. Thymin is 5-methyl uracil. It will also be noted that uracil and cytosin are corresponding oxy- and amino-compounds.

Pyrimidin groups exist as such in the nucleic-acid molecule; they are not derivatives of the purins. Thymin and cytosin are certainly primary products. It is possible that uracil is secondary to cytosin, but this is not probable (W. Jones). In discussing the structure of the mononucleotides and of the nucleosides, the part played by the pyrimidin-groups has already been made clear (see above).

**Free pyrimidins** (cytosin, thymin, and uracil), injected subcutaneously into dogs and rabbits, are recoverable from the urine; the animals are unable to alter them, the tissues not possessing the power either of demethylization, or of deamination, of these substances when free. Despite this fact, pyrimidins are not found in the urine after feeding nucleic acid, which indicates that they must be altered in the body while existing in combined form (Mendel and Myers). This alteration does not occur, however, while the substances are in the form of nucleosides (Levene and La Forge).

A new interest attaches to pyrimidin-derivatives through the studies of Funk on the so-called **vitamines**. Funk has prepared from yeast a pyrimidin derivative that he asserts will cure the polyneuritis of birds induced by a diet of polished rice (See Beriberi). He had earlier found in rice-polishings a substance that had the formula $C_{17}H_{20}N_2O_7$, and this may be identical with the pyrimidin derivative mentioned. If this observation be confirmed, it will represent a discovery of fundamental importance.

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### (f) *The Carbohydrates of the Nucleic Acids*

It has long been known that nucleic acid contains a *carbohydrate group,* but the exact nature of this group was long misunderstood. Recent studies have revealed the fact, already mentioned, that the carbohydrate group of animal nucleic acid is entirely different from that of plant nucleic acid; in the former, it is a *hexose,* while in the latter, it is a *pentose.*

#### i. The Hexose of Thymus Nucleic Acid

The carbohydrate group that has been obtained from animal nucleic acid is **levulinic acid** or *beta-acetyl-propionic acid:* $CH_3CO.CH_2.CH_2.CO_2H$.

It probably arises as a secondary product from a *hexose* group in thymus nucleic acid, though just what this hexose group is, is not yet certain.

#### ii. The Pentose of Plant Nucleic Acid

The nucleotides of yeast nucleic acid are compounds, in which, as we have seen, a phosphoric acid group is combined by means of a carbohydrate link with either a purin or a pyrimidin group; thus:

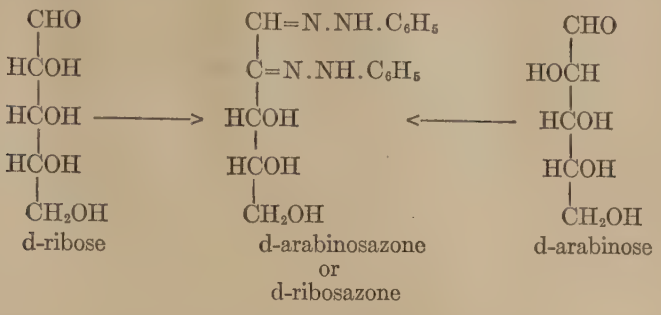
Phosphoric acid—carbohydrate—purin (or pyrimidin).

It turns out that the carbohydrate group of plant nucleic acid is a *pentose,* not a hexose.

No less than eight aldo-pentoses are known theoretically to be possible. Of these, it was, for a time, thought that the pentose of nucleic acid is *l-xylose, dl-arabinose* or *d-lyxose,* but the substance has finally been obtained in crystalline form by Levene and Jacobs, who have definitely demonstrated it to be **d-ribose,** which had not before been actually shown to exist.

This *d-ribose* is the only pentose that is found in the tissues of the animal body, and it is the pentose of plant nucleic acid. Obviously, it has a wide physiological distribution in vegetable and animal life. Its corresponding alcohol is adonite, the only pentite known to occur in nature.

The structural formula of *d-ribose,* of *its osazone* (the latter being identical with d-arabinosazone), and of *d-arabinose,* are as follows:




On oxidation, d-ribose yields *inactive trioxyglutaric acid,* while d-arabinose yields active trioxyglutaric acid. Crystals of d-ribose have been prepared by Levene and Jacobs.

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## (*g*) *The Ferments Responsible for the Catabolism of Nucleic Acid and Its Derivatives, Including the Purins*

Biochemical studies have gradually made clear to us the mode in which nucleic acid is physiologically decomposed in the body. It has been demonstrated that certain ferments are responsible for the cleavage.

It was formerly supposed that a single ferment, nuclease, attacks the nucleic acid and completely decomposes it into its final hydrolytic products. More recent studies, however, show that at least several different ferments are successively necessary in the process of degradation.

### i. Nucleinase, Nucleotidases and Nucleosidases

It seems probable from the studies of Levene and Medigreceanu, that plant nucleic acid is physiologically decomposed in **three stages.**

In the *first stage,* the yeast nucleic acid, which is a tetranucleotide, is decomposed by a ferment called **nucleinase** or **tetranuclease** first into two *dinucleotides* (Jones) and then into four *mononucleotides.*

In the *second stage,* these four mononucleotides (two of which are purin nucleotides and two are pyrimidin nucleotides) lose their phos-

phoric acid through the action of four specific ferments called **nucleotidases,** with formation of four corresponding *nucleosides.*

According to Walter Jones, each of the two purin nucleotides may undergo enzymatic decomposition in two different ways, for either one of two ferments may act; thus, phosphoric acid may be split off with formation of the purin nucleoside by means of a ferment called **phospho-nuclease**, or, purin bases may first be set free by means of a ferment known as **purin nuclease.**[1] In case phospho-nuclease acts, we have the formation, in one instance, of guanosin, and, in the other, of adenosin. In case purin-nuclease acts, guanin and adenin are formed, and the nucleosides are d-ribose-phosphoric acids.

In the *third stage,* the nucleosides are broken up into the carbohydrate portion (pentose) and a base (purin base or pyrimidin base, respectively), through the action of ferments called **nucleosidases.** These nucleosidases are *hydrolases* since they cause hydrolysis of the nucleosides with formation of the free bases.

For the purin nucleosides, no less than four different hydrolases are concerned.

Thus, **guanosin-hydrolase** splits *guanosin,* setting free *guanin* (Jones and Belt); **adenosin-hydrolase** splits *adenosin* setting free *adenin* (Amberg and Jones); **xanthosin-hydrolase** hydrolyzes *xanthosin* setting free xanthin (Jones); and, fourthly, **inosin-hydrolase** hydrolyzes *inosin,* setting free *hypoxanthin* (Levene and Medigreceanu; Amberg and Jones).

None of these ferments (nucleinase, nucleotidases, nucleosidases) is present in the succus gastricus or in the succus pancreaticus, but the succus entericus contains nucleinase and the two nucleotidases that attack the purin nucleotides. *Extracts of intestinal mucosa* contain nucleinase and all four nucleotidases, as well as the nucleosidases that decompose the purin-nucleosides, but no ferments that attack the pyrimidin-nucleosides. *Plasma from certain organs* (kidney, liver, heart, muscle) possess ferments of the same character as those in the intestinal mucosa, but *plasma from the pancreas, blood serum,* and *hemolysed blood,* contain only *nucleinase.*

Animal nucleic acid undergoes changes similar to those of plant nucleic acid, breaking up into nucleotides and nucleosides, but seems to be more resistant to fermentation.

### ii. The Deaminases

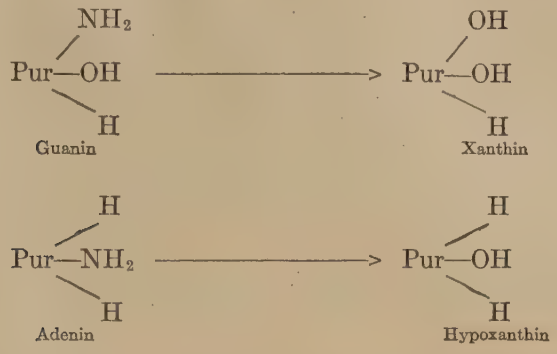
In the further degradation of nucleic acid, after the purin-base stage has been reached with formation of guanin and adenin, other ferments are concerned.

The aminopurins, under the influence of **deaminases** are changed into

[1] Might it not be better to use the terms phospho-nucleotidase and purin-nucleotidase?

their corresponding oxypurins. Thus, the aminopurin, *guanin,* is converted into the oxypurin, *xanthin,* by means of a ferment known as **guanase** (Jones and Partridge), and *adenin* is converted into *hypoxanthin* by means of another ferment, namely, **adenase** (Jones and Winternitz).

The reactions are indicated by the following formulae:



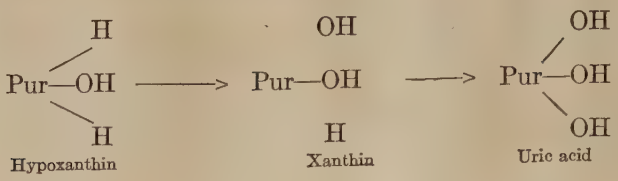

The proof of the independence of these two deaminases (guanase and adenase) has been successfully brought and the distribution of these ferments in the organs of men and animals has been carefully studied.

It has been found further that the guanin- and the adenin-groups can be deaminized while in the nucleoside molecule, but not by guanase and adenase. Still other ferments are involved; thus, for the deaminization of guanosin there is a special ferment, **guanosin-deaminase** (Jones), and for adenosin there is an **adenosin-deaminase.** These two aminopurin-nucleosides, are, on deaminization, converted into the corresponding oxypurin nucleosides, thus *guanosin* goes to *xanthosin,* and *adenosin* to *inosin.* We have already seen how xanthosin goes further to xanthin, and inosin to hypoxanthin under the influence of hydrolases (See above).

The study of the *distribution* of these ferments in the several organs of different animals, though difficult, yields interesting results. Apparently, the sites of these ferments vary for different animals. Thus, *dog's liver* is said to contain guanase, but not adenase; *pig's spleen* contains adenase, but not guanase (Jones and Austrian); *ox spleen* can deaminize both aminopurins (Spitzer, Schittenhelm), but this is because it contains the two deaminases (Jones). The deficiency of pigs' organs in guanase may account for the well-known deposits of guanin (often seen in ham), called "guanin gout." In human beings, *adenase* is not present in any of the organs; *guanase* is present in the kidney, liver and lung, but not in the spleen or pancreas.

### iii. Xanthin-oxidase

The very important ferment known as xanthin-oxidase (Spitzer; Wiener) is capable of oxidizing *hypoxanthin* to *xanthin,* and *xanthin,* in turn, to *uric acid.* The change can be indicated thus:




This ferment, xanthin-oxidase, is entirely independent of the deaminases and of the hydrolases described above. In human beings, xanthin-oxidase has been found in only one organ, namely, the liver. *Apparently, therefore, the liver is the great manufactory of uric acid in human beings, for it seems to be the only organ in which hypoxanthin can be oxidized to xanthin, and also the only organ in which xanthin can be oxidized to uric acid.*

In animals, xanthin-oxidase may be present in organs other than the liver; it is, for instance, an important ferment in ox-spleen.

### iv. Uricase

The organs of many animals contain a uricolytic ferment, known as **uricase**, which can destroy uric acid, oxidizing it to form **allantoin** and $CO_2$ (Cohn, Minkowski, Wiener, Wiechowski). It may be presumed to be present in organ-extracts, when, in them, uric acid destruction and allantoin-production occur simultaneously. Uricase is one of the *oxidases*, and is *thermolabile*. It is present in the liver of horse, cat, dog and rabbit, and in the kidney of the ox and the horse.

The end-product of purin metabolism in animals like the *dog*, *cat* and *rabbit* is therefore allantoin; it appears in large quantities in the urine after nucleic acid is fed to them

In *man*, uricase is not present, and so, after human beings ingest much nucleic acid, large quantities of uric acid are excreted in the urine.

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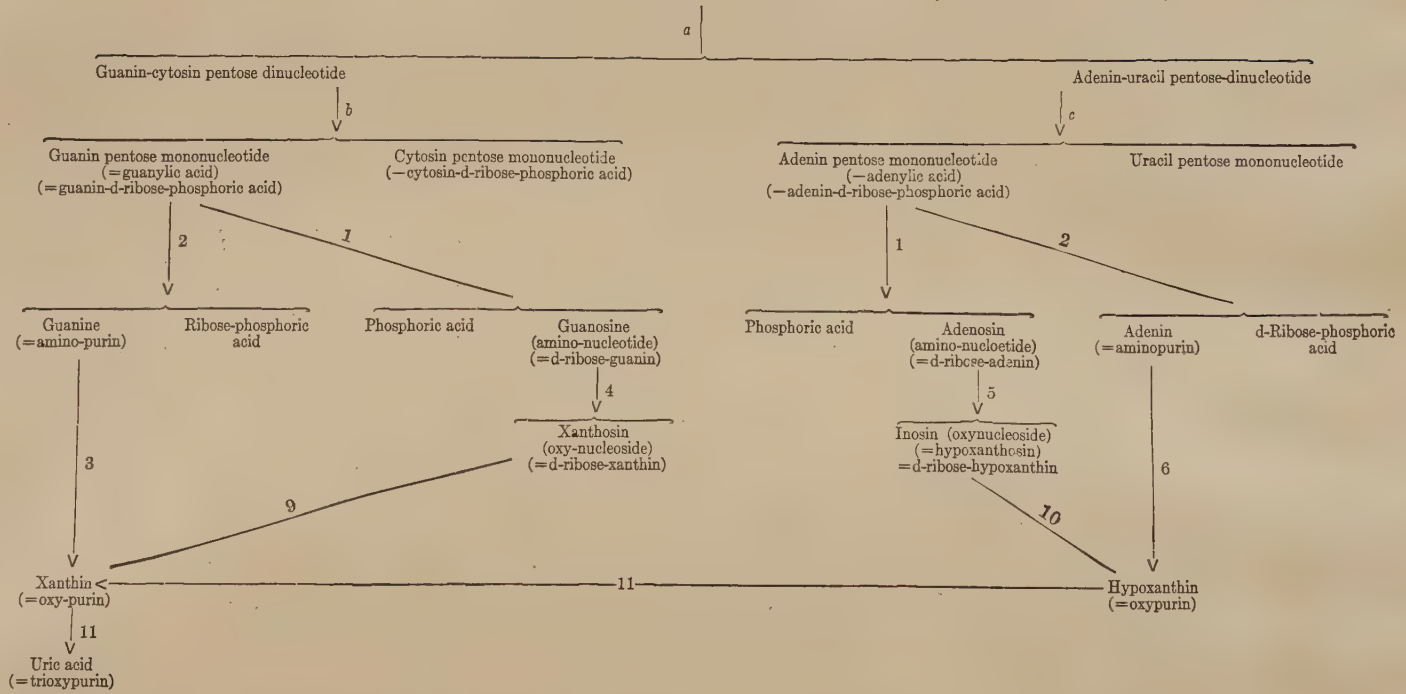
### *(h) Résumé of the Catabolism of the Nucleic Acids*

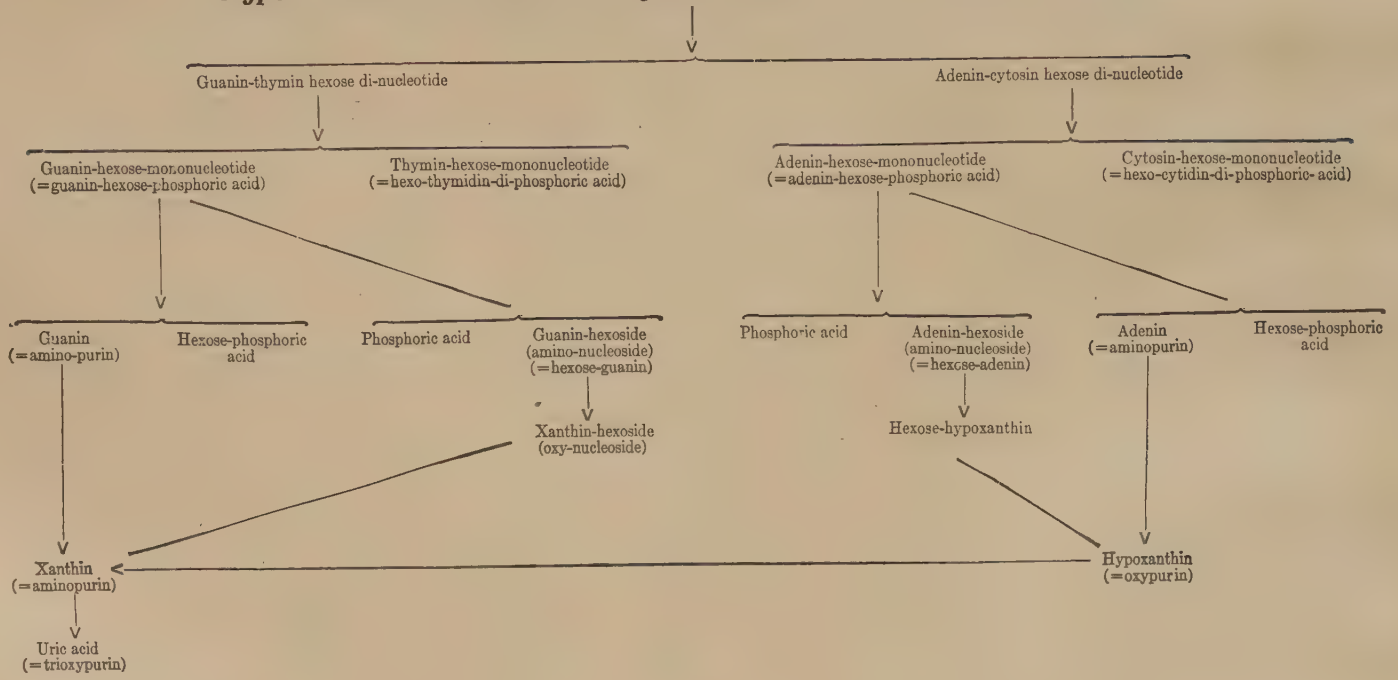
We are now prepared to take a bird's-eye-view of the whole series of transformations of purin compounds involved in the degradation of the nucleic acids by ferments. The two following diagrams will be easily understood by anyone who has read and understood what has preceded.

## *Probable Mode of Catabolism of Yeast Nucleic Acid (=tetranucleotide)*




The ferments concerned are indicated by letters or figures. Thus: *a*, tetranuclease; *b* and *c*, dinucleotidases; 1, phospho-nucleotidase; 2, purin-nucleotidase; 3, guanase; 4, guanosin-deaminase; 5, adenosin-deaminase; 6, adenase; 7, guanosin-hydrolase; 8, adenosin-hydrolase; 9, xanthosin-hydrolase; 10, inosin-hydrolase; 11, xanthin-oxidase.

***Hypothetical Catabolism of Thymus Nucleic Acid* (=*tetranucleotide*)**



### (i) The Purins of the Food Ingested

The purins of the food include: (1) those of plant nucleic acid (in the nuclei of vegetable cells); (2) those of animal nucleic acid (in the nuclei of animal cells in meat, fowl, fish, and especially in cell-rich foods like sweetbreads, liver and kidneys; (3) extranuclear mononucleotides in ingested glands and meat (guanylic acid, inosinic acid); (4) free hypoxanthin in meat; (5) trace of other free purins in meat (*e. g.*, guanin in pork); and (6) the methylpurins in tea, coffee and cocoa (theophyllin, caffein, theobromin). Small portions of the ingested purins are excreted in the feces.

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### (j) The Purins of the Urine

The purins of human urine consist chiefly of uric acid. Small quantities of three of the purin bases, namely, xanthin, hypoxanthin, and adenin are present also, but no guanin.

#### i. The Uric Acid of Human Urine

The uric acid of the urine is, in part, derived from those purins of the food (See above) that undergo physiological decomposition in the body, with formation of aminopurins (guanin and adenin) that are deaminized to form the oxypurins (xanthin and hypoxanthin), the latter in turn being oxidized in the liver to uric acid, which is given over to the blood and excreted in the urine. This uric acid derived from the food ingested is the so-called **exogenous uric acid.** The amount of it depends upon the purin-content of the food, and upon the regularity or irregularity of the processes of nucleic-acid and purin metabolism within the body.

The other part of the uric acid of the urine is derived from catabolism of the purin-containing compounds of the tissues of the body itself, including (1) the catabolism of the nucleic acids of the nuclei of the leukocytes

and of the cells of the organs and tissues generally, (2) the catabolism of the extranuclear mononucleotides (guanylic acid, inosinic acid) of the glands and of the muscles, (3) the catabolism of the free hypoxanthin of muscle. It is possible that, in addition, a little uric acid is directly synthesized in the body and excreted as such, though there is certainly no large synthetic production in man comparable with that in birds. The uric acid of the urine derived from the purins of the body itself is called **endogenous uric acid.** The quantity varies for different people, but is fairly constant for a given person (See Examination of Urine, Part IX).

### ii. The Purin Bases of Human Urine

Kruger and Salomon collected 10,000 liters of human urine, and from this amount prepared nearly 100 *g.* of purin bases, which they analyzed chemically with the following result:

| | |
|---|---|
| Methylpurins | 72.34 *g.* |
| Xanthin | 10.11 *g.* |
| Hypoxanthin | 8.50 *g.* |
| Adenin | 3.54 *g.* |
| Guanin | 0.00 *g.* |
| | 94.49 *g.* |

The **methylpurins** consisted of 1-methyl-xanthin, 7-methyl-xanthin (or heteroxanthin), 1-7-dimethyl-xanthin (or para-xanthin) and 7-methyl-guanin (or epiguanin). These methylpurins doubtless had their origin in the methylpurins of the food (chiefly, tea, coffee, etc., to a slight extent in other methylated purins of the food); they are independent of the ordinary metabolism of nucleins and the non-methylated purins of the food.

The presence of small quantities of the **oxypurins,** xanthin and hypoxanthin, in the urine are probably due to the fact that, xanthin-oxidase existing in the liver, small quantities of these oxypurins (both of exogenous and endogenous origin) escape conversion to uric acid under its influence and are excreted in the urine.

It will be noticed that of the **aminopurins,** guanin and adenin, the former is entirely absent from human urine, the latter present in minute amounts. We know that these aminopurins can both be deaminized while in a combined state in the human body, and guanin can be deaminized in a free state by guanase, but adenin in a free state cannot be deaminized because the ferment, adenase, present in the organs of many animals, is entirely absent from human organs (See above). Now in the food ingested, traces of *free* guanin and *free* adenin occur (autolysis of food), and in the alimentary canal some guanin and some adenin are set free (Walker Hall). These free aminopurins are partly excreted in the feces, partly absorbed into the circulation. Any free guanin absorbed is completely converted under the influence of the widely-distributed ferment guanase into the oxypurin xanthin, and so none will be left for excretion in the urine. Any free adenin absorbed will, however, owing to the entire absence of adenase in the human body, escape conversion, and will be excreted in the urine.[1]

[1] For an admirable presentation of the whole subject of the chemistry of the nucleic acids, the purins, and the various ferments that affect them, consult the monograph by Walter Jones, 1914. See References.

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[Note.—See also references in Part IX.]

## 4. The Metabolism of Creatin and Creatinin

The formulae of these substances have been given under the section on the Physiological Chemistry of the Proteins. We now know, however, that the metabolism of **creatin** and **creatinin** occupies a unique position, and deserves consideration separate from the metabolism both of the proteins and of the purins. The main facts known at present regarding this metabolism have already been discussed (See Part VII and Part IX).

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## 5. The Metabolism of Carbohydrates

### (a) The Chemistry of the Carbohydrates

Under this heading we include, the *sugars, glycuronic acid, glyoxylic acid,* and the *amino sugars* (especially glucosamin, kytin and chondroitin sulphuric acid).

The old term *carbohydrate* referred to substances, the molecules of which contain a molecule of water for each carbon atom present. As chemistry developed, it soon became clear that such a definition would include a large number of wholly unrelated substances, so that, recently, the term "carbohydrate" has been limited

to the *sugars* and their complex *derivatives*. As a matter of fact, some of the latter do not conform to the original definition of carbohydrate. The old term carbohydrate has come, therefore, to have only a *physiological* significance; it includes a group of chemical substances very important for the body, especially the sugars.

### i. The Simple Sugars

The *simpler sugars* include the *oxyaldehyds*, or **aldoses**, and the *oxyketones*, or **ketoses**. These sugars consist of *chains* of carbon atoms to which hydrogen atoms, hydroxyl groups, and, sometimes, unoxidized methyl-groups, are attached. The chains contain from 3 to 10 carbon atoms, though the sugars with which we have to deal in the body consist usually of chains of 6 carbon atoms, less often of 5 or of 3.

According to the number of oxidized carbon atoms in the chain, the sugars are designated, *dioses, trioses, tetroses, pentoses, hexoses,* etc., up to *decoses;* and according as the single groups are aldehyd-groups or keto-groups, we use names like *aldopentose, ketohexose,* etc.

**Dioses.**—Glycol aldehyd ($CH_2OH.COH$) is the simplest oxyaldehyd known.

**Trioses.**—Glycerin aldehyd ($CH_2OH.CHOH.CHO$), and an isomeric body, dioxyketone ($CH_2OH.CO.CH_2OH$) are probably important in synthetic processes in the body.

**Tetroses.**—These do not occur in nature, but have been made synthetically.

**Pentoses.**—The pentoses are important sugars, both for animals and plants, but especially for plants. Thus far *ribose, arabinose,* and *xylose* have been studied in relation to metabolism.

It has long been known that *nuclein* contains a carbohydrate group, which was believed to be a pentose. Recently, it has been shown that there are two nucleic acids, entirely different from one another; namely, *plant nucleic acid* and *animal nucleic acid.* The carbohydrate group of plant nucleic acid has been shown conclusively to be *d-ribose;* the carbohydrate of animal nucleic acid is not a pentose, but a *hexose,* related to levulinic acid. (See Nucleic acid metabolism.)

Theoretically 14 pentoses can exist; namely, six aldopentoses, four 2-ketopentoses, and four 3-ketopentoses.

The **pentoses of the urine** may be derived either from the pentose of the body metabolism, which is always *d-ribose* and is derived either from plant nucleic acid or ingested plant nuclei, or from extranuclear mononucleotides of the animal, like guanylic acid of the pancreas and other glands, and inosinic acid of muscle. Normally, the pentoses of this origin are fully oxidized in the body and do not appear in the urine.

Pentoses of plant origin, other than those contained in nucleic acid, may consist of the optically inactive *d, l-arabinose* or the optically active *l-arabinose* and *l-xylose.*

Pentoses occur especially in *fruits* (apples, cherries, plums, etc.). They may also result from the bacterial decomposition of other carbohydrates. These vegetable pentoses may be partially oxidized in the body,

but are often excreted in the urine. **Alimentary pentosuria** may occur in any normal person who happens to eat fruit rich in pentoses.

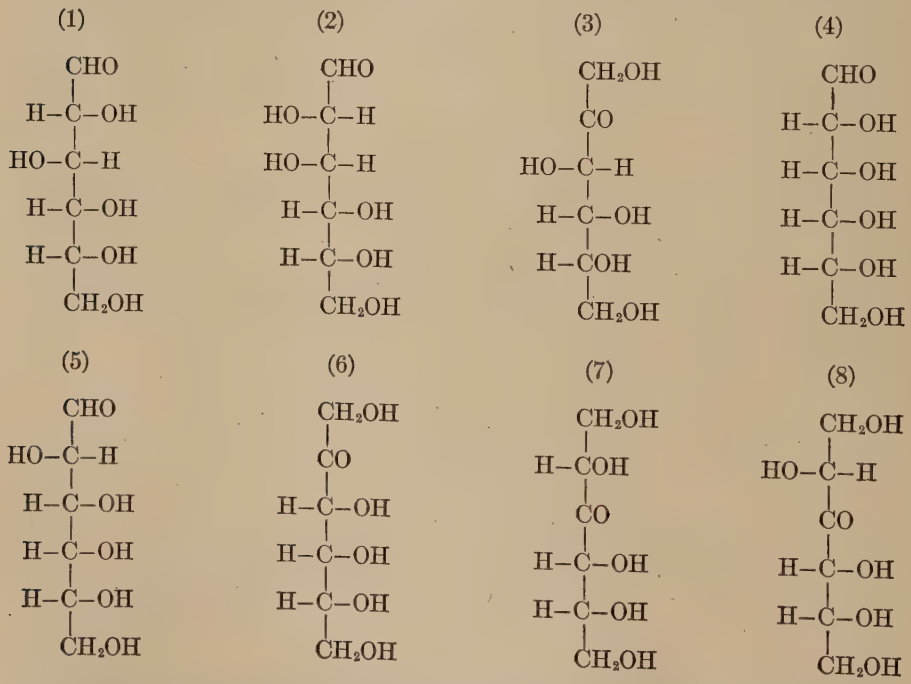
The **chronic pentosuria** reported in human beings, in which considerable quantities of pentose are excreted, are due to some inborn error of metabolism (Garrod). The origin of this endogenous pentose has not yet been satisfactorily studied. The disease occurs in families and appears to be harmless. I should not be surprised if the substance turned out to be *d-ribose.*

The formulae of d-ribose and d-arabinose have already been given (See Metabolism of Nucleic Acid and Purins).

**Hexoses.**—These are the most important sugars in nature, forming, as they do, the main source of energy for the animal body. The hexoses proper are *monosaccharides,* and consist of aldohexoses or *aldoses,* and ketohexoses or *ketoses.* Theoretically, no less than 32 isomeric hexoses of the formula $C_6H_{12}O_6$ exist.

These may be subdivided *into four natural series* of eight members each: (1) the *d-glucose* series, (2) the *l-glucose* series (mirror-image of (1) ), (3) the *d-galactose* series, and (4) the *l-galactose* series (mirror-image of (3) ).

To illustrate, the structural formulae of the d-glucose series is as follows:




In this series it will be observed that numbers 1, 2, 4 and 5 contain the *aldehyd group* at the end of the chain; they are, accordingly, called aldohexoses. Numbers 3 and 6 contain the *ketone group* at the second carbon atom and are therefore

known as 2-ketohexoses; numbers 7 and 8 have ketone groups at the third carbon atom and are therefore known as 3-ketohexoses. Of the *32 hexoses* there are altogether 16 aldohexoses, 8 2-ketohexoses, and 8 3-ketohexoses.

The sugars are feeble acids. They form salts with metals and therefore undergo slight ionization. They are also polyatomic alcohols, and, as we have seen, are either aldehyds or ketones. It is not surprising, therefore, that in their chemical reactions these sugars show a behavior that corresponds more or less to all three classes of compounds.

For the complex chemical reactions of the sugars, the papers of Nef and of Neuberg should be studied. Excellent epitomes of sugar chemistry will be found in Woodyatt's article in Wells' Chemical Pathology, and in the monographs of Armstrong and of Ling. (See References.)

### ii. The Complex Sugars

The hexoses may unite with one another in chains to form *disaccharids* and *polysaccharids*. Of the disaccharids, ordinary cane sugar or *saccharose,* ordinary milk sugar or *lactose,* and *maltose* are the most important in studies of metabolism.

Of the polysaccharids, ordinary vegetable *starch* and its derivative, *dextrin,* and animal starch, or *glycogen,* are the most important in metabolism.

*Cellulose* is also a polysaccharid, which cannot be split by animal ferments, though it undergoes a certain amount of cleavage as a result of bacterial fermentation in the intestine. On hydrolysis with acids it yields glucose.

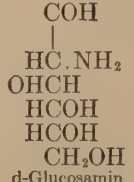
### iii. Glycuronic Acid

This is an aldehyd acid $CHO.(CHOH)_4.COOH$, which is derived from glucose. It occurs in normal and in pathological urines. It may occur free, but is usually united with aromatic alcohols or phenols to form *glucosids.* As has been seen in Section IX, the formation of such glucosids is an important detoxicating function of the body. These glucosids are sometimes spoken of as *paired* or *conjugated* glycuronic acids. The latter, when present in the urine, are not capable of reducing by themselves, but if heated with acids, the glucosid undergoes cleavage and the free glycuronic acid then acts as a reducing agent. It is sometimes mistaken in the urine for sugar. The glucosids formed by glycuronic acid are *levorotary* and can be precipitated with lead-acetate; free glycuronic acid, on the other hand, is *dextrorotary.*

### iv. The Amino Sugars

It is probable that the amino sugars play an important part in metabolism, representing a transition from the amino acids of protein to the carbohydrates. As studies in diabetes have shown, carbohydrate can be formed in the body from protein, and it may be that the amino sugars represent an intermediate stage in this process.

The best known body of this group is the amine of glucose, or **glucosamin.**




d-Glucosamin

Its osazone is identical with glucosazone. When it occurs in the urine, it appears as a formyl-compound; it yields the well-known Ehrlich-reaction with dimethylaminobenzolaldehyd. Taken into the animal body it is excreted unchanged in the urine.

F. Müller's studies on sputum indicate that *mucus* has a large glucosamin-content.

**Chitin,** which occurs in the protective covering of crustaceae, for example, in soft crabs, is a complex compound in which glucosamin is united with acetyl-compounds.

In this connection **chondroitin-sulphuric acid,** a complex sulphur body, which is abundant in cartilage, may be mentioned. It has been shown to contain an amino sugar.

### (*b*) *The Principal Carbohydrates of Interest for Human Metabolism*

The *principal carbohydrates,* then, that we have to consider, and some of their main characteristics, are illustrated in the following table:

**I. Monosaccharids.**

(A) Pentoses ($C_5H_{10}O_5$).

(1) *d-ribose.*
(2) *d, l-arabinose.*
(3) *l-xylose.*

(B) Hexoses ($C_6H_{12}O_6$).

(a) Aldohexoses (aldoses).

(1) *d-glucose* (dextrose or grape sugar): dextrorotary; reduces; is fermented with yeast.
(2) *d-galactose:* dextrorotary; reduces; is not fermented with pure beer yeast; does not occur free.

(b) Ketohexoses (ketoses).

(1) *d-fructose* (levulose or fruit sugar): levorotary; reduces; is fermented with yeast.

**II. Disaccharids** ($C_{12}H_{22}O_{11}$).

(1) *Saccharose* (cane sugar): dextrorotary; does not reduce; is not fermented with beer yeast. On cleavage, it yields d-glucose (dextrose) + d-fructose (levulose).

(2) *Lactose* (milk sugar): dextrorotary; reduces; is not fermented with yeast; on cleavage, it yields d-glucose (dextrose) and d-galactose.

(3) *Maltose:* dextrorotary; reduces; is fermented with yeast; on cleavage, it yields 2 molecules of d-glucose (dextrose).

**III. Polysaccharids** $(C_6H_{13}O_5)n$.

(1) *Starch* (amylum): swells in water; is not fermented with yeast; does not reduce; on digestion (by amylases), it yields dextrin, maltose and d-glucose (dextrose).

(2) *Dextrins*: partly soluble in water, are not fermented with yeast; do not reduce; on cleavage, they yield d-glucose (dextrose).

(3) *Glycogen* (animal starch): opalescent solution in water; dextrorotary; is not fermented by yeast; does not reduce copper; on cleavage, it yields first dextrin, later d-glucose.

(4) *Cellulose:* insoluble in water, dilute acids or dilute alkalies; not split by animal ferments; split in alimentary tract to some extent by bacteria, with formation of volatile fatty acids, methane, and $CO_2$. On hydrolysis with acids, it yields d-glucose.

Carbohydrates are formed synthetically in green plants, where chlorophyll, with the aid of sunlight, is able to build sugar from carbon dioxid and water, the chlorophyll acting as an accelerator of the reaction (catalyzer). The carbon dioxid is reduced first to formaldehyd, and then, step by step, carbohydrate chains are formed until the hexoses, starches and celluloses are reached.

### (c) *Digestion and Absorption of Carbohydrates in the Human Body*

The carbohydrates of the food consist of *monosaccharids* (glucose, levulose, mannose, galactose), *disaccharids* (cane sugar, milk sugar, maltose), and *polysaccharids* (starch, glycogen, dextrin, cellulose, inulin, vegetable gums), and certain *pentoses,* especially in the nucleic acids and in fruits (see above). Of all these, the polysaccharid, starch, makes up the major portion of the carbohydrates of the food.

**Digestion.**—The monosaccharids do not need to be changed during digestion, since they can be absorbed as such.

The disaccharids and polysaccharids, however, must undergo cleavage through the action of the digestive juices before they can be absorbed. The cleavage occurs as the result of the action of the *amylase,* ptyalin, of the saliva and of the ferments of the pancreatic and intestinal juices (*invertase, lactase, maltase, amylase, dextrinase*).

The polysaccharids, especially starch, begin to break down during insalivation in the mouth cavity, passing through the stages of erythrodextrin, achroödextrin and isomaltose into maltose. The process continues to a certain extent, though it is considerably inhibited, in the stomach, and is taken up again vigorously in the intestine, where the alkali of the pancreatic juice neutralizes the HCl of the gastric juice.

Maltase, as we have seen, changes the maltose into d-glucose.

Cellulose is not attacked by the digestive secretions, though a certain amount is disintegrated by bacterial activity within the intestine. The pentoses of the food are taken in chiefly in cherries, plums, strawberries and blackberries, though wine and beer have a considerable pentose content. In all vegetable nuclei, the nucleic acid molecule contains a pentose group. In animal nuclei, the nucleic acid contains a hexose group.

**Absorption.**—On absorption, the carbohydrates enter the portal circulation and pass directly to the liver; only a very small amount, if any, is absorbed by way of the lymphatics and the thoracic duct.

### (*d*) *The Formation of Glycogen*

On reaching the *liver,* the sugar is caught and stored up in that organ, the liver being a *warehouse* for carbohydrate, on the one hand preventing an excess of carbohydrate from entering the blood, and, on the other, by a regulatory mechanism, providing that the sugar-content of the blood is maintained always at a certain level. In the warehousing of the sugar, the monosaccharid d-glucose is polymerized in the form of its anhydrid, *glycogen.*

The **glycogen,** formed synthetically in the *liver,* is deposited in the protoplasm of the cells, not in the cell-nucleus. Aside from the liver, the *muscles* also act as a storehouse for glycogen, this substance being stored up in the muscle-fibrils, in the interfibrillary cement-substance, and in the sarcolemma. Glycogen of muscle is not transported to it as such, but is synthesized in the muscle from the d-glucose of the blood. During *starvation,* the glycogen supply of the liver is used up first, the musculature containing still considerable amounts of glycogen after the liver has become glycogen-free.

Of the *monosaccharids,* d-glucose, levulose and galactose can be directly synthesized into glycogen. Of the *disaccharids,* cane sugar cannot be converted into glycogen unless it has previously undergone cleavage within the intestinal canal to form d-glucose and levulose. Cane sugar, introduced by the parenteral route, is recoverable, quantitatively, in the urine. Similarly, maltose must undergo cleavage, though the ferment maltase is present not only in the intestinal canal, but also in the blood; hence maltose, introduced by the parenteral route, need not appear in the urine. Lactose must be split into d-glucose and galactose by the ferment lactase of the intestine in order that glycogen may be formed from it. Lactose, introduced by the parenteral route, reappears, quantitatively, in the urine; it is used, in this way, as a test of renal function (see Part X).

Of the *polysaccharids,* starch, in order to be utilized for glycogen-formation, must undergo complete cleavage into d-glucose in the intestine.

Of the *pentoses,* none is capable, so far as is known, of forming glycogen.

### (*e*) *The Conversion of Glycogen into d-Glucose*

In order that the stored glycogen of the liver and of the muscles can be used in the body, it must be re-transformed into sugar. This trans-

formation depends upon the activity of an *amylase.* The origin of this amylase, or diastase, is not entirely clear. Some have sought it in the liver cells themselves, but the majority of investigators think it arrives in the liver and in the muscles through the blood and the lymph.

The sugar formed from glycogen and given over to the blood is believed to be *d-glucose* (or dextrose). There has been considerable discussion as to whether the d-glucose is free, or in the form of jecorin, or other loose combination. In the tissue-cells, the sugar (probably after preliminary dissociation) is burned to carbon dioxid and water, through the action of *oxidases* within the cells.

If sugar be offered by the portal blood in too great quantity, or too rapidly, to the liver, the latter is unable to catch all of it and convert it into glycogen. The excess passes over into the blood and gives rise to *hyperglycemia.* Whenever a hyperglycemia exists, a regulatory function of the kidneys sets in, and the sugar is excreted in the urine (*glycosuria*). Glycosuria due to this cause is known as *alimentary glycosuria.* The body has only a certain tolerance for carbohydrate taken in as food. When this tolerance is exceeded, alimentary glycosuria appears (See Tests).

Apparently, however, the animal body cannot produce alimentary glycosuria simply by the ingestion of starch, since starch-cleavage within, and absorption from, the intestine require so much time that the sugar-content of the portal blood never exceeds the capacity of the liver for *glycogenogeny,* but if cane sugar, or glucose, be ingested beyond a certain amount, alimentary glycosuria appears, even in normal persons (See Part IX).

### *(f) Sources of Glycogen and of d-Glucose Within the Body Other Than the Food Ingested*

Aside from the principal origin of glycogen in the carbohydrates of the food, sugar may also arise from the protein and fat of the food or of the body. This has been proven experimentally in animals, and is also clear from studies on diabetes in man (*q. v.*), as well as in the experimental diabetes of animals (Minkowski). The main source of **sugar from protein** undoubtedly lies in the utilization of the fatty-acid moiety of the amino acids after deaminization.

F. Müller's studies on lysin, and F. Kraus' studies on alanin, led the way to a whole series of investigations that have made sugar-formation from the amino acids of protein clearer.

Theoretically, **sugar from fat,** may arise, either from the glycerin-content of fat, though the amount of this is small (Lusk), or from the fatty acids themselves (Ringer). While the evidence for the origin of

sugar from fat is not so satisfactory as for the origin of sugar from protein, still studies in diabetes (von Noorden), and experimental studies, make it seem probable that some sugar in the body may, under pathological circumstances at any rate, be derived from fat.

**Alcohol,** when taken in as food, is probably utilized as such in combination, and not converted into carbohydrate.

### (*g*) *The Catabolism of the Sugars in the Body*

We have seen that glycogen is broken down in the liver and the muscles, as required, to maintain a tolerably constant sugar-content in the blood, by means of an amylase (glycogenase), which converts it into d-glucose. This *mobilization of sugar* seems to depend, in part at any rate, upon the activity of the sympathetic nervous system under the stimulation of *epinephrin* (= adrenalin).

Claude Bernard's *piqûre* consisted of puncture of the floor of the fourth ventricle between the points of origin of the auditory nerve and of the vagus nerve. It is followed by a hyperglycemia and a glycosuria, which continues until the glycogen of the liver is reduced to a low percentage. It seems probable that the area in the medulla oblongata receives afferent impulses chiefly through the N. vagus, and sends efferent impulses through the spinal cord to the upper portion of the pars thoracalis; thence through the rami communicantes to the inferior cervical and superior thoracic ganglia of the N. sympathicus to reach the liver by way of the N. splanchnicus. It is possible that the splanchnic impulses either increase the glycogenase of the liver directly (McLeod), or indirectly, through stimulating the adrenals to increased secretion of epinephrin (von Noorden).

But **how glucose is actually utilized in the body** and finally oxidized to carbon dioxid and water, is still far from clear. Some light is being thrown upon the process by the chemical studies of sugars in alkaline solutions. Since sugars are feeble acids, they form salts with metals, and it is possible that they undergo *ionization* like other salts (A. P. Mathews, Michaelis). The glucose-anion is then subject to cleavage and intramolecular rearrangement. According to Nef, a dissociation of the sugar known as *methylene-dissociation* occurs previous to other transformations (intramolecular rearrangements, oxidations). Woodyatt has brought forward strong evidence in favor of the view that chemical dissociation of glucose in the body is a normal occurrence, for instance, in the formation of lactic acid from glucose in muscle, and he believes that *failure of glucose dissociation* will explain all the metabolic phenomena of diabetes "more directly and simply than any other single physiologic error that has been hypothecated." This view is compatible with the fact that sugars other than d-glucose may be utilized in diabetes. The undissociated glucose, being incapable of combustion, of polymerization into glycogen, or of reduction to fat, would accumulate in the form of

chemically inert molecules in the cells and fluids of the body, maintaining a hyperglycemia and a glycosuria.

Other theories of the mode of utilization of d-glucose have been put forward; thus, it has been assumed that the pancreas secretes an oxidizing ferment (*glucase*) that directly oxidizes d-glucose (Lepine).

Again, it has been assumed that the body must be able, in some way, to *"fix glycogen"* previous to the utilization of its sugar (Naunyn). *Inability thus to fix the glycogen* is designated "diszoamylie"; as a result of this disability, the other metabolic disturbances of diabetes are, according to Naunyn, sequences.

Still another view is that the body must incorporate sugar in a *colloidal union* that permits of its transportation to points of utilization and prevents its too early excretion (Pavy). According to the latter view, the assimilation of sugar takes place in the intestinal villi and the lymphocytes are the morphological elements that carry the sugar.

A view that for some time received credence was that of Cohnheim, according to which glycolysis occurs in muscle as a result of enzyme activity, but for the activation of the enzyme in muscle some *kinase* has to be supplied by the pancreas.

Finally, Allen has suggested that sugar must undergo some form of colloidal combination in the blood, and that for this purpose an *"amboceptor"* supplied by the pancreas is essential.

It has been mentioned above that when the blood sugar exceeds a certain amount (*hyperglycemia*), sugar appears in the urine (*glycosuria*). There is another condition in which sugar appears in the urine in the absence of hyperglycemia; namely, a condition in which the cells of the kidney are altered in such a way as to lead to "a disturbance of equilibrium whereby the relative blood sugar and urinary sugar concentrations are altered in favor of the urine." This change in the cells of the kidney can be easily brought about in experimental animals by the administration of phlorhizin, either by the mouth, or, more markedly, by subcutaneous injections. The condition is known as **phlorhizin-diabetes.**

The relation of **glycuronic acid** to the normal catabolism of glucose is not fully understood. Glycuronic acid occurs normally, but may appear in the urine in increased amounts in various intoxications, probably owing to the fact that, normally, most of it goes on to further oxidation, whereas in these pathological states it is caught up out of intermediary metabolism to de-toxicate poisons. The relations of glycuronic acid to d-glucose are easily seen from the accompanying formula:

$$\underset{\text{Glucose}}{OHC.(CHOH)_4.CH_2OH} + O_2 = \underset{\text{Glycuronic acid}}{OHC.(CHOH)_4.COOH} + H_2O$$

Ordinarily, an aldehyd group is more easily oxidized than an alcohol group, so that it would seem likely that the oxidation of glucose to glycuronic acid occurs while the aldehyd group of glucose is occupied, owing to combination with some other substance, thus escaping oxidation. For the conjugated glycuronic acids see Part IX (Examination of the Urine).

A word must be said regarding **levulinic acid.** This substance has been found among the degradation products of thymus nucleic acid. It is beta-acetyl-propionic acid ($CH_3CO.CH_2.CH_2.CO_2H$). It is regarded as a secondary product formed from a hexose group in the nucleic acid molecule. What this hexose is, is not yet certain. It stands in the same relation to thymus nucleic acid and other animal nucleic acids, as does the pentose, d-ribose, to yeast nucleic acid and other vegetable nucleic acids. It is probable that levulinic acid is catabolized like other hexoses in the body.

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## 6. The Metabolism of Fats

### (*a*) *Résumé of the Chemistry of the Fats*

The fats of the human body and of the bodies of animals are *esters of glycerin,* that is, all three hydroxyl groups of the tri-atomic alcohol, glycerin, are replaced by acid radicles, the fats themselves being **triglycerids.** The fatty acids concerned are *palmitic acid, stearic acid* and *oleic acid.* In the fats of milk, esters of lower fatty acids (*butyric acid, capronic acid,* etc.) also occur. As an example of such a triglycerid, the formula of *tripalmitin* may be given:

$$\begin{array}{l} CH_2.O.C_{16}H_{33}O_2 \\ | \\ CH.\ O.C_{16}H_{33}O_2 \\ | \\ CH_2.O.C_{16}H_{33}O_2 \end{array}$$

In animal fats, the three glycerides, *tripalmitin, tristearin* and *triolein* are present in variable amounts, and since these three fats have different melting points, we can easily account for the differences in melting points of animal fats.

The *melting points of single fats* are as follows:

Tripalmitin, 65.5° C.; tristearin, 71.5° C.; triolein, —4° C.

Some of the vegetable fats (*e. g.,* olive oil, cotton-seed oil) resemble animal fats. Fats rich in oleic acid are fluid (oils) or have a very low melting point. Goose

fat is an example. Fats rich in tristearin, like beef tallow, have a higher melting point. The fats obtained in the kitchen, through extraction by melting ("trying-out" or "rendering" fat), are impure, since they are admixtures of genuine fats with lipoids and coloring matters. The pure fats can be extracted from the mixture with ether.

Fats are soluble in ether, in hot alcohol, benzol, chloroform and ligroin. They are insoluble in water and in salt solutions.

When over-heated in the air (above 200° C.), they begin to decompose and give off an acrid odor due to the formation of *acrolein* from *glycerin*. This test distinguishes true fats from mineral oils, vaselin, etc., which are paraffins (saturated hydrocarbons).

When the fats become rancid, the odor is due chiefly to oxidation products of oleic acid.

Fats undergo **cleavage** into *glycerin* and *fatty acids* (oleic, stearic, palmitic) when chemically treated in various ways. This process, known as **saponification of fats,** occurs also during the digestion of fat through the action of ferments known as the **lipases.** Salts of the fatty acids with alkalis (*e. g.,* potassium oleate) are known as **soaps.**

### (*b*) *Criteria for Recognition of the Fats*

On studying the fats physically and chemically, it has been found too difficult, practically, to isolate the single constituents, but we can recognize the different fats by paying attention to certain criteria that permit of comparison and differentiation. These include:

(1) The determination of the **melting point**; beef fat or suet melts at about 45° C.; pork fat or lard at about 40° C.; goose fat at about 32° C.

It is convenient to remember that mixtures of tripalmitin and tristearin melt between 62° and 69° C. If fat contain over 50 per cent triolein, the melting point will be depressed to about 51° C.

(2) **The acid number.**—Most fats contain some free fatty acid and are hence capable of absorbing a slight amount of alkali before yielding an alkaline color reaction with phenolphthalein. The number of milligrams of KOH necessary to make the fat alkaline with phenolphthalein as indicator is called the *acid number,* which is obviously a measure for the *content in free fatty acids.*

To determine the acid number, the fat is dissolved in alcohol and ether, and alcoholic KOH is added until the phenolphthalein is reddened. One gram of beef tallow has an acid number of 0.5.

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 g of beef tallow | has | an | acid | number | of | 0.5 -10 mg. KOH. |
| 1 g of lard | " | " | " | " | " | 1 -20 mg. KOH. |
| 1 g human fat | " | " | " | " | " | 2 mg. KOH. |

(3) **The saponification number.**—This informs us regarding the *amount of neutral esters* present in the fat. It is expressed as milligrams of KOH required to neutralize the fatty acids that are set free upon saponification. The fats are saponified by means of alcoholic KOH and heat, and the excess of KOH is titrated back with HCl.

The saponification number for ordinary fats is about 196 mg. KOH for 1 g. of fat. Fats like butter, and certain vegetable fats, have lower numbers, probably because in addition to their triglycerids they contain cholesterin and higher alcohols.

Pure triglycerids have the following saponification numbers: Palmitin, 209; stearin, 189; olein, 190.

(4) **The iodin number.**—This informs us regarding the *amount of unsaturated fatty acids* present. It is the amount of iodin in per cent of weight of the fat that the fat can take up.

To an alcoholic solution of fat we add a solution of iodin and mercuric chlorid in alcohol, and titrate back the excess of iodin with thiosulphate.

Since 1 g. triolein can combine with 0.86 gram iodin, the iodin number of triolein is 86.

The iodin numbers of tallow and lard and other animal fats vary with their content in olein. The value for beef tallow is 40, for lard 50-70, for butter 30.

(5) **Reichert-Meissl number.**—This informs us regarding the *amount of volatile fatty acids* that can be driven off with steam. The number is expressed in cubic centimeters of N/10 KOH necessary to neutralize the fatty acids in 5 g. of fat after saponifying and acidifying with steam. The number is most used in examining butter, which has a larger content in the lower fatty acids than have other fats. Thus, the Reichert-Meissl number for butter is 20-33, for tallow and lard about 1.

(6) **The acetyl number.**—This informs us regarding the *presence of hydroxyl groups* (alcohols, oxyacids). It is not much used in the study of the higher fats.

For the isolation of the single constituents of fats, chemical methods are valuable, but are difficult of application. The reader is referred to the excellent monograph by J. B. Leathes.

### (c) *Digestion and Absorption of Fats*

The fat taken in as food (fats of meat, butter, milk, olive oil, etc.) are but little altered in the stomach. On reaching the intestine the fat is *emulsified* by the bile and pancreatic juice. A minute amount is absorbed by the intestinal wall unchanged, but most of the fat is *split* by means of the ferment **lipase** into fatty acids and glycerin. The fatty acids unite with alkalis to form neutral soaps. These are transported through the lymph channels and thoracic duct to the left subclavian vein, and are distributed to the tissues, where they are stored up until required as fuel by the body.

**The Catabolism of Fats.**—When fat is burned in the body, it is *first split* into fatty acids and glycerin by means of lipases. But the *intermediate stages* down to $CO_2$ and water are not known. Some of the fat may be converted into *sugar* before it is burned.

On *oxidation* of the fatty acids, it is believed that the second carbon atom from the carboxyl (the so-called beta carbon atom) is first attacked, the fatty acids becoming *keto-acids* in this way.

Thus, *butyric acid* ($CH_3.CH_2.CH_2.COOH$), when oxidized at the beta carbon atom, becomes $CH_3.CO.CH_2.COOH$, which is *aceto-acetic acid*, or *diacetic acid*.

Similarly, it is believed that keto-acids are formed from the higher fatty acids, after which the chain breaks down at the level of the keto-group, with formation of acetic acid and a fatty acid shorter by 2 carbon atoms; the latter can in turn become oxidized again at the beta carbon atom, and so the long carbon chain

of the higher fatty acid is gradually broken up into simple bodies (See Acetone Bodies).

Just how the fats give rise to *sugars* under certain circumstances (*e. g.,* in diabetes) is not yet known.

It is known that the fats play a part in the formation of certain important chemical substances of the tissues, including (1) the *phosphatids* of the central nervous system (lecithin; cerebrin), (2) *cholesterin,* and (3) the *bile acids.* The chemistry of the intermediary processes has, however, not yet been worked out.

The human *intestine* can absorb large amounts of fat, though the maximum for 24 hours is about 300 g. Some fat is discharged with the feces unabsorbed. The loss of fat in bacon is 12.6 per cent, in yolk of egg, 4.4 per cent, in the fat of milk, 4.5 per cent, and of butter, 4.1 per cent (Rubner).

Fat injected *subcutaneously* is absorbed and used in metabolism, but only very slowly; thus, of 500 grams of oil injected subcutaneously, only 2-3 grams will be utilized in metabolism per day. According to Winternitz, not more than 20-25 calories daily can arise from the burning of fat injected subcutaneously. From nutrient enemata, about 10 grams of fat per day can be absorbed (Duecher).

### (*d*) *Sources of the Fat of the Body*

The fat of the body is derived from the *fats* of the food, from the *carbohydrates* of the food, and from the *protein* of the food or of the body.

As has been pointed out, most of the *fat taken in as food* undergoes cleavage and is absorbed as soaps and glycerin. When re-synthesized in the body, the fats peculiar to the body are formed. There is evidence, however, that *foreign fats,* entirely different from the normal fat of the body, can be absorbed as such and deposited in the tissues as foreign fat, where it may remain, at least for weeks, unchanged (Rosenfeld). When fat is needed, this foreign fat can be used in metabolism, apparently like normal human fat.

The *fat derived from the carbohydrates of the food* differs somewhat from the fat of the body derived from the fat of the food, containing less oleic acid.

The *fat derived from protein* of the food and of the body has its source in the deaminized residues of the constituent amino acids of protein, which, as we have already seen, are utilized also in the formation of sugar. The fat of so-called *fatty degeneration,* seen in the protoplasm of the cells of glands, is, in all probability, not fat arising *in loco* from the protein, but is fat that has wandered in from fat depots elsewhere in the body; in other words, what was formerly described as fatty degeneration of cells appears to be in reality a *fatty infiltration* (G. Rosenfeld).

### (*e*) *Storage of Fat in the Body*

The main *depots for the storage of fat* in the body are the subcutaneous tissues, the omentum and mesentery, and, to a certain extent, the interstitial tissues of the organs. A certain amount of fat can be stored in the liver cells. The fat stored in the liver remains there only tempora-

rily, while the great fat depots (subcutaneous tissue, peritoneum) serve as more permanent warehouses for fat.

When the liver-cells are well supplied with glycogen, they do not store fat, but if the glycogen-content fall, fat begins to wander into the liver-cells from the fat depots of the body.

### (*f*) *The Acetone Bodies*

Among the acetone bodies we include: (1) *beta-oxybutyric acid;* (2) *diacetic acid,* and (3) *acetone.*

#### i. Chemistry of the Acetone Bodies

The relation of these substances to one another will be easily seen by the structural formulae. Thus, the mother substance, **beta-oxybutyric acid,** has the formula:

$$CH_3—CH—OH—CH_2—COOH.$$

On oxidation, this gives rise to **diacetic acid,** or **aceto-acetic acid—**

$$CH_3—CO—CH_2—COOH,$$

which, in turn, breaks up into $CO_2$ and **acetone:**

$$CH_3—CO—CH_2—COOH = CH_3—CO—CH_3+CO_2.$$

*Acetone* is a ketone; *diacetic acid* is a ketonic acid, and *beta-oxybutyric acid* is a monobasic oxyacid.

#### ii. The Acetone Bodies in Intermediary Metabolism

These acetone bodies are not present in the normal urine, since normally they are not end-products, but intermediary products of metabolism. Under pathological conditions, however, they may appear in the urine, and acetone is sometimes excreted in the breath (see Diabetes).

Physiological chemists are almost unanimous in the opinion that *diacetic acid,* at any rate, is normally present in intermediary metabolism, arising during the catabolism of the fatty-acid chains of fat, and during the catabolism of the nitrogen-free residues of the deaminized amino acids of protein. But, in normal metabolism, diacetic acid is itself catabolized, being either directly oxidized to $CO_2$ and $H_2O$, or re-synthesized to form sugar. *Acetone* is probably a secondary product derived from diacetic acid through cleavage of the latter into acetone and $CO_2$.

The relation of diacetic acid to *beta-oxybutyric acid* is still in dispute. Formerly, it was believed that *beta-oxybutyric acid* is the primary substance, or mother substance, and that diacetic acid is derived from it as a secondary product due to oxidation. One thing is certain, however, from recent studies, namely, that beta-oxybutyric acid can be formed from diacetic acid in the body by *reduction,* and can then be excreted in the urine. Some believe that beta-oxybutyric acid always has this origin. Others assume that either body may be easily formed from the other (reversible reaction), and that, according to circumstances, the formation of the one or the other body will predominate.

### iii. Acidosis and Acetonuria

The conditions under which acetone bodies appear in the urine are referred to in Part IX. They include the **acidosis** of *diabetes* and that of *inanition,* for apparently the catabolism of fats is interfered with when carbohydrates are not being normally utilized in metabolism. In diabetes, sugar cannot be utilized, and the acetone bodies accumulate in the blood. In *prolonged vomiting,* and in *starvation,* the sugar supply is so cut down that the fats cannot be utilized and the acetone bodies accumulate in the blood and are excreted in the urine **(acetonuria).**

### iv. Ketogenous and Antiketogenous Substances

Much experimental work has been done with the object of determining what substances, when fed under the abnormal conditions in which acidosis occurs, favor the formation of the acetone bodies, and what substances are antagonistic to such formation. These substances are known as *ketogenous* and *antiketogenous* substances, respectively.

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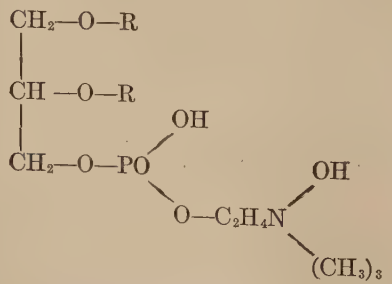
## 7. The Metabolism of Lipoids

By lipoids are meant substances that can be extracted from cells by means of ether. The ether extract represents a complex mixture of substances. Aside from the neutral fats present in such an ethereal extract, two large groups of substances are distinguishable: (1) the *phosphatids,* and (2) the *cholesterins.* In addition, though less abundant, the extract contains (3) the phosphorus-free *cerebrosids,* or aminolipoids, and (4) the pigments known as *lipochromes.*

### (*a*) *The Phosphatids*

These are complex substances in which *glycerin* is combined with *phosphoric acid,* a *base,* and a *fatty-acid radicle.* According to the content of the molecule in P and N atoms, we speak of mono-amino-monophosphatids, triamino-diphosphatids, and the like.

The most important phosphatid in metabolic studies is **lecithin.** Lecithin is, however, not a single body, but a group of several mono-amino-monophosphatids, since the fatty-acid radicle of the lecithin molecule in the different lecithins varies. The substances are so closely related to one another, however, that they are considered together under the designation "lecithin." In lecithin, *glycerinophosphoric acid* is combined with *cholin,* and with *two* variable *fatty-acid radicles,* according to the general formula:




Lecithin is present in all the cells of the body. In the food it is an important constituent of yolk of egg. It is a *colloid,* intermediary in position between a suspensoid and an emulsoid, and, like the proteins, behaves as an *amphoteric elec-*

*trolyte,* forming loose combinations with protein (*lecithalbumins*). Like other colloids, it swells up in water. The lecithins undergo cleavage through the action of specific ferments (*lecithinases*), breaking down into their components (fatty acids; glycerino-phosphoric acid; cholin). Free **cholin** *is* known to be present in the blood and to have a vagotonic effect; it is thus an antagonist of epinephrin.

It has been suggested that lecithin may unite with glucose to form *glucosids,* and that the sugar of the blood may circulate largely in the form of some such glucosid. For a time it was thought that *jecorin* is such a glucosid, but the existence of typical lecithin-glucosids is uncertain; the substances taken to be such may have been mere *adsorption phenomena,* so characteristic of colloids. The relation of the lecithin of the red blood corpuscles to intoxication with *snake venom* (Kyes), has been referred to in Part IV.

Among the other phosphatids of the body may be mentioned the *cephalin* of the brain and kidney, the *myelins,* the *sphingomyelins,* and *sahidin* of the nervous system. These are of physiological interest, but thus far cannot be valued for clinical studies of metabolism. The same may be said of the phosphorus-free *aminolipoids* or *cerebrosids.*

### (*b*) *The Cholesterins*

The *cholesterins* are chemically not related to the phosphatids, though they are included in the group of lipoids. Chemically they consist of complicated hydrated carbon rings and are grouped among the hydroaromatic substances.

Cholesterin is widespread in the human body, making up about 20 per cent of the dry substance of the *white matter* of the brain. It is also an important constituent of the *bile* and of *gall-stones.* Cholesterin *esters* (oleate, stearate) are present in the circulating blood and in the cells of the kidney.

Cholesterin is a *secondary alcohol* of a complicated, doubly-methylated ring system known as *cholesten.*

The *coprosterin* of human feces yields the color reactions of cholesterin, and is probably one of its reduction products.

The *bile acids* are probably derived from cholesterin, consisting, as they do, of hydrated benzol nuclei.

*Glycocholic* and *taurocholic acids* are the two principal bile acids, though several others have been demonstrated in human bile. In *fatty degeneration* of the organs, the cholesterin-content is increased. Cholesterin seems to possess the property of inhibiting the activation of hemolytic substances by lecithin.

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# 8. The Metabolism of Inorganic Substances (Mineral Metabolism)

## (a) *The Significance of Mineral Matter in Metabolism*

Inorganic constituents of the body tissues are found in various combinations, and the significance of each form is quite different. We may mention some of the different forms.

### i. Forms in which Inorganic Materials are Found in the Body

1. Large **deposits of insoluble inorganic material** (calcium, phosphorus, fluorin, magnesium, etc.) are present in the bones and in the teeth. Aside from their mechanical functions, these deposits in skeletal structures must be looked upon as reserve depots whence, in time of need, the more active tissues may obtain the requisite amount of these inorganic elements.

2. Sulphur, phosphorus, iron, iodin, and other less common elements, are found firmly combined in certain **organic molecules.** These inorganic elements have here no function as electrolytes, but they determine very largely the properties of these organic molecules. The iron in *hemoglobin,* for instance, allows hemoglobin to take up and to lose oxygen. Other examples of such combinations of inorganic elements in organic molecules are met with in *casein, nucleic acid, phosphatids,* and *thyroglobulin.*

3. Another organic combination in which inorganic material is found in the tissues is as **"protein salts,"** formed by the union of acids or bases with proteins, since proteins (chains of amino acids) by virtue of their amino groups, on the one hand, and of their carboxyl groups, on the other, can unite with either acids or bases. It is doubtful whether neutral salts can form such combinations with protein. The importance of these combinations lies in the aid they offer in maintaining the neutral reaction of the body fluids.

4. Finally, inorganic elements are found as **free soluble salts** (electrolytes). The chief *cations* of these electrolytes are sodium, calcium, potassium, magnesium, and the chief *anions,* chlorids, sulphates, phosphates, and carbonates.

### ii. Functions of Salts and of Ions

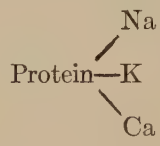
The very important rôle of such salts in the living body is far from being clearly understood. It is evident that they *regulate the reaction* of the body fluids and tissues. The ingestion or formation in metabolism of the inorganic anions, $SO_4''$, $Cl'$, etc., and of organic acids, is balanced in part by the ingestion of the cations $Na^{\cdot}$, $K^{\cdot}$, etc., and in part by the formation of the cation $NH_4^{\cdot}$ in the body (see Reaction of the Urine).

Another physico-chemical activity of these ionized salts consists in maintaining a level of *osmotic pressure* most suited to the various cellular activities. The relation of osmotic pressure to distribution of fluids in the tissues and to the processes of resorption and secretion is a very direct one.

Perhaps even more important, though little understood, are the *interrelationships of the electrolytes and the great mass of bodies that are*

*present in a colloidal condition.* Emulsion colloids, such as are of chief interest in this connection, undergo *gel-formation* under the influence of electrolytes, the reversible or irreversible nature of this change of state depending in part upon the character of the cations concerned, in part upon the type of colloid. Again, the *hydrophile action* of colloids, that is, their affinity for water, is strongly affected by the electrolytes present in the solution. Finally, the *protective action of certain colloids on hypersaturated solutions of salts*, preventing precipitation, may be cited as still another example of the complex interrelationships between colloids and salts that exert an important influence upon the vital processes in the body.

Certain ions possess powers more specific than those mentioned above that are due to the common properties of all electrolytes. There is evidence that different functions demand for their performance the presence of certain ions in a definite proportion (*ion-balance*). The contraction of muscle tissue, for instance, has been shown to demand the presence of a certain amount of sodium; whereas, if potassium be increased, this function is antagonized. Loeb has suggested that we have in cells a *protein-ion compound* of the type




The ions joined to the protein may be characteristic of the tissue. If an excess of one of these ions occurs in the surrounding fluid, it may displace the others by mass action, thus yielding a protein-ion combination of abnormal character. The details of such reactions are of course hypothetical; but the importance of the rôle of the electrolyte may be summed up in Mann's words: "So-called pure ash-free proteins are chemically inert, and, in the true sense of the word, dead bodies. What puts life into them is the presence of electrolytes."

### iii. Effects of an Ash-free, or of a Salt-free, Diet

It has been shown experimentally (Taylor, Forster) that the ingestion of a *diet free from inorganic salts* rapidly results in symptoms of grave nutritional derangement and causes death more quickly than does absolute starvation. The human, like the animal, organism needs inorganic salts; if it does not get them in sufficient amounts, **"salt-hunger"** develops. This hunger for inorganic salts will develop more quickly on a diet of vegetable than on one of animal food. Vegetable foods, it is true, contain more "ash" than animal foods, but "ash-content" and "content in dissolved and dissociable inorganic salts" are not synonymous

(Köppe); apparently much of the mineral content of plants exists in organic combination.

### (*b*) *Factors Affecting Mineral Metabolism*

#### i. Mineral Constituents of the Food Ingested

The inorganic constituents of a mixed diet are present in much the same variety of forms as we have just seen are characteristic of the inorganic elements as they occur in the body.

Thus, there are *insoluble salts* such as calcium phosphate, elements firmly bound in *organic combinations* such as iron in casein, or sulphur in cystin, and *soluble, free salts,* such as are present in mineral waters.

In general these free salts are of *three types:* "(1) neutral inorganic electrolytes, especially chlorids; (2) vegetable salts of the alkali and earthy metals, carbonates, acetates, tartrates, citrates, etc., which are present rather abundantly, and (3) acid phosphates, which are present in comparatively small amounts. Were the salts of these three types removed from an ordinary mixed diet, then thoroughly mixed and allowed to come to equilibrium, we would find that the reaction would be rather strongly alkaline" (Hawk). This balance on the alkaline side is needed to neutralize the sulphuric acid formed in the body from the sulphur ingested in protein combination, as well as other acid bodies of metabolic derivation.

#### ii. Absorption of Mineral Constituents

The extent to which certain inorganic constituents of the diet, especially phosphorus, iron, and sulphur, are freed from organic combinations before resorption has been a subject much discussed. It now seems probable that *phosphorus* is resorbed chiefly as salts of phosphoric acid, that *iron* in both inorganic and organic form can be taken up by the intestinal wall, that *sulphur* is resorbed both as sulphates and as the amino acid, cystin. In general, the *other inorganic cations and anions* are resorbed in inorganic combination. The chief *site* of the resorption is the small intestine.

#### iii. Distribution of the Several Mineral Constituents in the Tissues

In the tissues of the body, the salts are not uniformly distributed but show a tendency to be present in varied proportions. In the case of an element like *phosphorus*, which, in the body, is present in all nucleins, it is plain that the percentage of the element may vary in different tissues according to their richness in nuclear material. In the case of elements like *sodium* and *potassium*, which exist as ions not firmly combined, variations in the tissue content of these elements are attributable to physico-chemical processes characteristic of the particular tissue.

### iv. Excretion of Mineral Substances

The excretion of mineral matter is chiefly through the *urine* and *stools*, though appreciable amounts are to be found in the *sweat* and, exceptionally, in the *milk, sputum,* etc.

Gautier gives as the average excretion of mineral matter per day in the urine 17.3-22 gm.; in the feces, 4.35-6 gm.; in the sweat, 1.6-2.4 gm. It must not be assumed, however, that each mineral is excreted according to these proportions. On the contrary, the excretion of each tends to be individual. *Chlorids* are excreted almost entirely in the urine and sweat. *Iron* is eliminated almost entirely into the large intestine. *Phosphorus* and *calcium* are found in large amounts in both urine and feces.

### v. The Balance of Mineral Substances

In normal adults, the body tends to maintain an *equilibrium* between the total mineral intake and output. Moreover, a balance will usually be found to exist for the metabolism of each single element; but essential differences in character distinguish the mechanism of the balance in each case.

As an illustration, it will suffice, at this point, to cite the fact that whereas the ingestion of an excess of *sodium chlorid* is usually followed by rapid elimination of the excess with no disturbance of the chlorid balance, an ingested excess of *calcium lactate* may be retained through a period of many days, with a corresponding *positive balance*, which only very gradually gives way to a long period of elimination in which a *negative balance* obtains.

Another type of mineral balance of especial interest is that of *iron*, in which the intake and output are both small in spite of a very active internal synthesis and destruction of iron compounds. The explanation is that, in this case, there is an *internal circulation* of iron, this iron being repeatedly re-utilized.

Aside from these interesting individual types of mineral metabolism, it is to be noted that the *balance of total mineral metabolism* tends, under certain physiological conditions, to show variations. It has been shown, for instance, that in periods of *growth*, and during *pregnancy*, the mineral output is less than the mineral intake.

### vi. Mineral Metabolism in Pathological States

The study of the *disturbances of mineral metabolism* in various pathological conditions has not yet reached a stage in which many positive facts are agreed upon.

**Disturbances of Absorption.**—In disease, the *resorption of salts* shows abnormal variations, which at times are due to the ingestion, or forma-

tion in the intestines, of insoluble compounds. Thus, the calcium absorption may be diminished if a large amount of phosphates be simultaneously ingested, since the comparatively insoluble calcium phosphate is excreted in the stools. Intestinal troubles of various sorts apparently exert an influence upon the resorption of inorganic material; and an excess intake of certain salts predisposes, in itself, to intestinal irritation.

**Disturbances of Balance.**—Internal disorders that affect the balance of *intake* and *output* of all, or of one or more, of the mineral constituents of the body are discussed under the heading of the several mineral bodies (See Part IX) and in connection with special diseases (Parts XI, XIII and XIV). In general, they have been studied chiefly in relation to *pathological ossification* and *calcification* (Ca, Mg, $PO_4$), and in connection with the investigations of *acidosis,* of *edema,* of *nephritis,* and of certain *diseases of the glands of internal secretion* (*e. g.*, tetany).

**Disturbances of Elimination.**—The proportionate amounts of the same mineral body in the various excretions, urine, feces, sweat, etc., often show abnormal variations. In "PHOSPHATURIA," for example, the *calcium* output in the urine may be distinctly increased, while the calcium in the stool is correspondingly diminished in amount (Umber). This increase of calcium in the urine is an important factor in the precipitation of the phosphates. Such disturbances of mineral excretion are no doubt usually secondary to variations in unknown factors that determine the amounts excreted by each path.

In the case of minerals, such as *sulphur,* which is excreted in several forms (sulphates, ethereal sulphates, neutral sulphur), pathological conditions of metabolism may lead to an abnormal increase in one form at the expense of the others; as, for example, the increase of ethereal sulphates in phenol poisoning.

**Formation of Concretions.**—The formation of *concretions* is intimately allied with the excretion of mineral bodies. Calcium salts are those most commonly involved, but magnesium, sodium, potassium and ammonium salts may also be precipitated. The more common anions in concretions are phosphates, oxalates, carbonates, and urates. The amount of certain salts in the excretions is greater than could be dissolved in a like amount of distilled water. Urine, for example, is normally a *supersaturated solution* of calcium oxalate. The stability of such supersaturated solutions is due to the normal presence of "protective" colloids in the excretion. Such *colloids* greatly increase the power of the fluid to hold salts in solution. If, however, these colloids undergo *gel-formation* as a result of change in the reaction of the media, or of contact with other colloids of opposite electrical charge, the *salts are precipitated.* The conception of the formation of calculi as a simple precipitation from an aqueous solution of salts excreted in abnormal concentration must be enlarged to include the reciprocal relationships

of both salts and colloids in solution in all the excretions. The study of the urine and of the bile as colloidal solutions (Lichwitz, Schade, etc.) has already thrown much light on the formation of concretions.

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## 9. Water and Metabolism

This has already been discussed in part under Examination of the Urine (See Part IX). The reader may also consult "The Polyurias" and "Diabetes insipidus," which follow in the next section.

Of late years, clinicians have become greatly interested in following the "water balance" in various conditions.

### (*a*) *The Water Supply of the Body*

The *water supply* of the body has two sources: (1) *water* taken in as such; (2) water of *foods* including: (a) their *water content, e. g.,* in milk, beer, vegetables, etc.; (b) the *"oxidation water"* resulting from the oxidation of the H of carbohydrates, fats and proteins in intermediary metabolism. It has been estimated, that on a mixed diet ($\frac{1}{2}$ or more carbohydrate, $\frac{1}{6}$ protein, $\frac{1}{3}$ or less fat) 100 calories yield about 12 g. "oxidation water."

### (*b*) *The Water Output of the Body*

The *water output* of the body includes the water in: (1) the *urine* (varying in amount with that given off by the sweat and the expired air); (2) the *feces* (ordinarily, 60-120 g. water per day); (3) the *sweat;* (4) the *expired air;* and, to a slight extent, (5) the *sputum, sperm, menstrual fluid, nasal secretion,* and *tears.*

The *amount of sweat* varies enormously under different conditions (temperature and humidity of air, muscular activity, etc.). According to Atwater and Benedict, the normal body, *at rest* in a comfortable room, gives off nearly a liter (935 g.) of water as "insensible perspiration" by way of the skin (60 per cent) and the expired air (40 per cent). In *hard labor,* as much as 3 or even 8 liters may be given off by skin and lungs! Since such amounts exceed the urine output, the fallacy of trying to judge of a water-balance by following the amount of urine alone is obvious. In following a water-balance, the control of the urine should be accompanied at least by the daily control of the body weight also.

The *blood* tends to constancy in its water content (males 76-80 per cent; females 77-81 per cent). In unusual pathological states, the blood may become less aqueous (75 per cent in cholera; 70 per cent in fatal burns).

When water intake is not followed at once by water output, the water is *stored,* not in the blood but (chiefly) in the muscles and in the fatty tissues. In pathological cases, the retention of water in the body results in the accumulation known as **"edema"** and **"dropsy"** (ascites, hydrothorax). These states are described elsewhere.

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## 10. Vitamins and Metabolism

One of the most astonishing discoveries of recent times is the demonstration that certain substances, entirely aside from the ordinary proteins, carbohydrates and fats, existing in the vegetable kingdom, are

necessary to the normal growth and nutrition of animal tissues. It has been shown that these substances, called **vitamins**, become a part of animal tissues, so that if fresh meat be eaten, or if unboiled milk be drunk in sufficient quantities, their direct ingestion from plants becomes unnecessary.

An absolutely *pure* mixture of protein, carbohydrates, fats and salts will not maintain life (Osborne and Mendel). In experiments on the growth of rats it was found that growth ceased when the fat in the diet consisted of lard, and rapid growth quickly set in when *butter fat* was substituted for the lard (Osborne and Mendel). This experiment brought the proof that *butter fat contains something necessary for growth that is not present in lard.*

The disease **beriberi** has long been known, especially among rice-eating peoples. Some peoples, however, like the Bengalese, whose diet consists largely of rice, do not suffer from beriberi. In 1897 Eijkman pointed out that beriberi occurs among rice-eating peoples only when the rice is prepared in a certain way. Thus, when the rice is milled by machinery, so as to be free from its husks or pericarp, and such rice forms the exclusive diet, beriberi develops almost with certainty; whereas, if the whole rice be eaten, or if rice polishings accompany the diet of milled rice, beriberi does not develop.

Chickens or pigeons fed on white rice (that is, polished rice) develop a *polyneuritis,* which causes general weakness and paralysis of the legs and wings, a disease picture similar to beriberi. Fed on whole rice, or upon polished rice with the addition of meat or beans to the diet, these fowl do not succumb.

Potatoes, many cereals, meats sterilized at high temperature, and boiled milk, do not contain enough vitamins to prevent neuritis (Funk).

An attempt has been made to *isolate the substances* that will prevent beriberi; thus, Funk, from 100 kilograms of dried yeast, prepared 1.6 grams of a crystalline substance that he asserts will, if given in doses of 4-8 mg. to neuritic pigeons, cure them in a few hours. On purifying this substance, he obtained three materials, which he designated *Substance 1*, *Substance 2*, and *nicotinic acid.* He found that *Substance 2* is entirely inactive. *Substance 1* given alone, and *nicotinic acid* given alone, have but little effect on the polyneuritis of birds, but if he gives 3 mg. of *Substance 1* and 2 mg. of *nicotinic acid* simultaneously, the diseased pigeons recover in a few hours. Funk asserts that the same two substances can be recovered from rice polishings. He is of the opinion that they are related to the *pyrimidins* (*q. v.*).

It is believed that in addition to beriberi, *scurvy,* and possibly *rickets* and *pellagra,* are also due to a one-sided diet; namely, to a deficiency in vitamins. Great care must be taken, however, in rushing to a conclusion regarding the etiology of these diseases. The idea is certainly a plausible one and should lead to profitable experimentation.

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## 11. The Total Metabolism

Since the fundamental studies of Pettenkofer and Voit in Munich, the interest of clinicians in the *total metabolism* in health and in disease has gradually increased until, today, some investigators devote themselves almost entirely to the study of the subject. In the United States, the studies of Atwater, Benedict, Lusk and DuBois have been especially fruitful. Sometimes the total metabolism is followed over a long period, 24 to 48 hours; sometimes over a shorter period, a half hour to 6 hours (see Methods in Section II).

### (a) *Data Required for Estimating Total Metabolism*

In studying the total metabolism for a **longer period** (of 24 hours or longer), the data required include: (1) a knowledge of the fuel value of

the food intake, (2) a chemical study of the excreta (*N* of the urine and feces; C of the expired air, urine and feces; and the $H_2O$ output). The study of the excreted nitrogen gives a clue to the protein metabolism, and that of the excreted carbon and hydrogen the clues to the combustion of carbohydrates and fats, since in a 24-hour period the oxidations can go as far as their end-products.

A comparison of the output with the intake permits a judgment to be formed regarding the metabolism that has taken place during the period. It is customary to measure the consumption of oxygen during respiration as well as the $CO_2$ of the expired air, since a study of the *relation of the oxygen-consumption to the $CO_2$-excretion* permits one to draw conclusions regarding the relative amounts of protein, fat, and carbohydrate, respectively, consumed.

A study over such a long period, though tolerably easy with animals, is extremely difficult to apply accurately to human beings, especially to people who are sick, and the expense of such studies makes them prohibitive in most clinics. In America, however, Atwater and Benedict, and, later, Benedict by himself, and Lusk have undertaken such studies on human beings, with results that must ultimately prove of great value.

For the study of **briefer periods,** the Zuntz-Geppert Apparatus and the Universal Respiration Apparatus are useful. By them, the consumption of oxygen and the excretion of $CO_2$ in the expired air are followed for short periods, and the relation of the two to one another is known as the

**respiratory quotient** $\left(\frac{CO_2}{O_2} \text{ value}\right)$

This quotient varies according to the kind of food (protein, carbohydrate, fat) that is undergoing combustion. Thus:

Respiratory quotient for starch = 1.
Respiratory quotient for protein = 0.793.
Respiratory quotient for fat = 0.707.

With the aid of such a method, we can determine the part taken by protein, fat and carbohydrate, severally, in the total metabolism. And, further, we can, by experimenting, study how the metabolism of the several foodstuffs is affected by influences such as the state of nutrition and muscular exercise, which, it is well known, cause alterations in the total metabolism.

### (*b*) *Factors Influencing the Total Metabolism*

The total metabolism of men and animals is not directly proportional to the *body weight,* for smaller animals catabolise more intensely than do

larger animals (Rubner). It has been found, however, that the total metabolism is directly proportional to the *body surface*, which, as is well known, is relatively greater in small animals than in large.

The body surface can be approximately calculated from v. Meh's formula:

$$\text{Surface} = K\sqrt[\frac{2}{3}]{a}.$$

The constant $K$ for human beings is 12.3, while $a$ is the body weight of the man, or of the animal under study. This formula gives the body surface in square meters.

In general, this surface law of Rubner holds, but there are certain exceptions to it, even in health; thus, *age* and *sex* have some influence, aside from the differences in the area of the body surface that they entail, and other studies indicate that the variable *activity of the endocrine glands,* in health and in disease, cause variations in the intensity of total metabolism.

In *children,* the total metabolism is more intense than at any other time in life. In *old age*, the total metabolism is decreased, and even to a greater extent than the loss of weight and the lessened exercise of the senile will account for.

Among *adults*, the total metabolism of the *resting-fasting individual* is constant for the single person, though it varies somewhat for different persons.

The marked influence of *muscular exercise* upon metabolism has already been referred to (See Fuel Value of the Foods). The energy for muscular contraction may be derived not only from carbohydrates and fats, but also from protein. Ordinarily, however, the body uses carbohydrates and fats as the source of this energy, proteins being called upon only under exceptional conditions. Obviously, therefore, laboring men require a much larger supply of carbohydrate and fat in their diet than do men whose occupations are sedentary.

The *quantity*, but more particularly the *quality, of the food ingested* has a definite influence upon the total metabolism. In the fasting-resting state the total metabolism quickly (12-14 hours) falls to a minimum (See Total Basal Metabolism). If now the influence of muscular exercise, of the outside temperature, and of other external stimuli be excluded, we can study the effects of the food intake, in short experiments, with the Zuntz-Geppert apparatus.

Such experiments have shown that the ingestion of *fat* causes only a slight increase of the total metabolism. *Carbohydrate* has a somewhat greater effect, but the ingestion of *protein* has a powerful effect, increasing the total metabolism as much as 20 per cent (in man), or even more in animals (Magnus-Levy). An *abundant mixed diet* increases the total metabolism (calculated for 24 hours) by about 13 per cent.

For a time it was thought that the increase in total metabolism following the ingestion of food was due to the work of digestion. While digestive activity undoubtedly plays a rôle in the increase of the oxidation process, it is by no means the main factor. We must, with Rubner, assume that the single foods act as *specific stimuli* to the oxidative processes in the cells of the organism, and that the increased activity excited is by far the greatest for protein (*specific dynamic action*).

The effects of *temperature* on total metabolism have also been carefully studied. It has been found that in animals heat regulation is maintained by chemical processes chiefly; they control their metabolism, especially the metabolism of fat, chiefly by means of muscular contractions (A. Löwy). In man, instead of this *chemical* regulation, a *physical* regulation prevails, for man protects himself less by alterations in the amount of heat produced than by diminishing the loss of heat (vasomotors of skin, evaporation from skin and lungs).

Exposure of the human body to *heat* does not seem to lessen metabolism; indeed, hot baths slightly increase total metabolism. If the baths be very hot, there may be a considerable increase.

The effect of *climate* upon total metabolism has been the object of a number of metabolic studies. Thus, in *mountain climates*, the total metabolism is increased, and in greater degree than the dyspnea will account for. The food intake is greater in the mountains than at the sea level. Left to themselves, people eat more carbohydrate and protein, though the amount of fat ingested remains practically unchanged. Muscular work increases total metabolism to somewhat greater degree at an altitude than at ordinary levels. Patients sent to convalesce in the mountains, especially if they are anemic or under-nourished, should eat plenty of protein (Richter).

In a *sea climate*, the total basal metabolism is somewhat increased, though there are marked individual differences, the increase being greater in some persons than in others (Löwy and Muller).

The effects of the endocrine glands upon total metabolism have already been mentioned. We know most about the effects of the secretion of the *thyroid gland*. As is well known, in hypothyroidism, the total metabolism is decreased and the patients tend to increase in weight, even when the diet is meager. In hyperthyroidism, on the contrary, the total metabolism is greatly accelerated, and a thin chit of a girl may eat as much as a man at hard labor and still lose weight. The thyroid secretion appears to act like a fan to the flame of the combustion processes in the body.

The internal secretion of the *gonads* appears also to exert an important influence upon total metabolism. Castration, or cöphorectomy, soon leads to a distinct reduction in total metabolism, as measured by the Zuntz-Geppert method. It is more marked in females than in males.

In the former, the administration of ovarian substance will increase the total metabolism after oöphorectomy. These considerations are of importance in connection with constitutional or endogenous obesity (*q. v.*).

# B. Methods of Investigating Metabolism

## 1. Introduction

The more comprehensive studies in metabolism, formerly confined to animal experiments in physiological laboratories, are rapidly being extended to man, and are now becoming a recognized part of the work of the medical clinics. It seems probable that in the near future every large hospital will have a department for the especial study of the diseases of metabolism. This would be a real help to the understanding of many conditions now obscure.

It is desirable to have patients that are under metabolic study in special rooms or wards, in which the food intake and the output of the urine and feces can be absolutely controlled by skilled nurses and orderlies under the supervision of medical men that have had special training in metabolic investigations. These conditions are at present unobtainable in ordinary hospital wards, and, indeed, anywhere in hospitals as at present organized. Connected with the metabolic wards there should be (1) suitable apparatus for indirect, and, if possible, also for direct calorimetry; (2) a chemical laboratory in which analyses of food, excreta and respiratory gases can be undertaken; and (3) a metabolic diet kitchen. As to the *methods* to be employed, they include:

1. Investigations of **total metabolism.** Here, exact determinations of (a) the total intake, (b) the total output, and (c) the oxygen-consumption and the carbon-dioxid elimination in respiration are made. The total metabolism may be *increased* (as in fever, in the cachexias, and in hyperthyroidism), or it may be *diminished* (as in obesity, in hypothyroidism, and in agenitalism).

2. Investigations of the **partial functions of metabolism.** Here, special studies of protein metabolism, nucleic acid metabolism, creatin and creatinin metabolism, carbohydrate metabolism, fat metabolism, lipoid metabolism, and mineral metabolism (salts and water) may have to be made. In such studies, the intake may be especially arranged as regards its content in the substances under consideration; and exact analyses of the urine and feces for these particular substances and their derivatives will be made.

Thus, for example, in studying *protein metabolism*, the N-intake and the N-output are exactly followed; in studying *nucleic acid metabolism*,

the exogenous and the endogenous purins are of especial interest; in studying *carbohydrate and fat metabolism,* the carbohydrate intake, the sugar output in the urine, if any, and the acetone bodies will be closely followed; whereas in studying *mineral metabolism,* the balance of one or more of the mineral salts, or the balance of water will be investigated by comparing output with intake.

In addition to quantitative determinations of the *normal end-products* of the different substances in the output, examinations will be made to determine, in the output (especially in the urine), the presence or absence of substances *intermediate* in position between the complex molecules of the food ingested and the simple end-products normally excreted. The appearance in the urine (or blood) of abnormal quantities of such intermediate substances is of great importance, since a study of them will often throw light upon the nature and location in the body of the diseases giving rise to disorders of metabolism. Thus the study of **intermediary metabolism** has revealed the existence of a series of remarkable *adaptive processes,* by means of which the body protects itself against *infectious agents,* and other *foreign substances* that gain entrance to it, and against *poisons* that enter from without or are produced within the body. Of such adaptive processes may be mentioned (1) the manufacture of the *defensive ferments* of Abderhalden and of the whole series of *antibodies* (antitoxins, lysins, etc.) described in Part IV; (2) the *de-toxication of benzoic acid and of phenol and cresol* by conjugation with glycocoll, with $H_2SO_4$ and with glycuronic acid, so that they are eliminated as hippuric acid, ethereal sulphates, and glucosids in the urine; and (3) the utilization of $NH_3$, as it is formed, as a *neutralizer of an excess* of *acids* (diacetic acid; beta-oxybutyric acid) in the blood, in order to keep an acid intoxication within bounds.

In the *cachexias* and in *fever,* the toxic destruction of protein may occur so rapidly that the body cannot maintain protein-equilibrium. In *diabetes mellitus,* the glucose molecule cannot be cleft; it accumulates in the blood (hyperglycemia) and is excreted in the urine (glycosuria). In *gout,* uric acid accumulates in the body and may be deposited in the joints or in other tissues (tophi). In *obesity,* the oxidative processes are diminished. In the *amino acid diatheses,* the metabolism of certain of the amino acids (cystin, phenylalanin) may be arrested or may follow abnormal paths. In *rickets* and in *osteomalacia,* the Ca and Mg balances are disturbed. In *diabetes insipidus,* the kidney is incapable of secreting a concentrated urine and so, adequately to eliminate the solids of the urine, an enormous secretion of water is necessary. In *beriberi,* the food is insufficient in vitamins and a polyneuritis develops. In the *endocrinopathies,* certain hormones are produced either in excess or in insufficient quantities (Addison's disease, Graves's disease, myxedema,. tetany, acromegaly, etc.).

In *uremia,* and in *cholemia,* chemical substances normally excreted can no longer be adequately eliminated; they accumulate in the blood and poison the cells, especially the neurones of the nervous system. Many other interesting examples might be cited, but these will suffice to indicate the great interest that attaches to studies of metabolism. Properly to investigate these various disorders of metabolism, it is necessary skillfully to apply a whole series of physical, chemical and biological methods of examination. Only the principal methods of proven clinical value can be referred to here. For the full details of these methods, and for methods not taken up here, the larger treatises on metabolism, and the special articles in the journals, should be consulted (See References).

The more important *chemical methods* used for studying the blood, the urine, the feces, etc., are either described or referred to in chapters dealing with these subjects (See Parts VII, VIII and IX). I shall give here, however, a list of references to some of the recent treatises on biochemistry.

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## 2. The Food Ingested and Its Analysis

Certain general rules should be observed on beginning a metabolic study:

1. The patient must be under the absolute control of the physician and his assistants during the period of metabolic study so that accurate knowledge concerning food intake, urine output, feces output, rest, exercise, emotion, etc., will be accessible.

2. All food ingested and all urine and feces excreted must be accurately weighed, or measured, and a record thereof kept.

3. A metabolic study to be of any value must permit of observation over a period long enough to make the necessary examinations.

### (*a*) *Arranging the Diet*

It is convenient to use a diet of constant composition and to give the same amount daily. When this is practicable it minimizes the amount of analytical chemical work required; in healthy persons this is easy, but in the sick it may be difficult to arrange such a constant diet without hardship to the patient.

#### i. Rough, Approximative Work

For preliminary orientation and for ordinary clinical purposes, where a more exact study is not indicated, or where it is not feasible, sufficient accuracy can often be arrived at by *calculating* the content of the food in its various constituents according to Schwenckenbecher's tables, Locke's "Food Values," or the analyses in König's treatise. One weighs the food used, and gives it to the patient. Should any part of the food remain uneaten, it must be weighed afterward and the amount subtracted from the original quantity. The food may be weighed either raw, or after preparation for the table, as analytical tables for both raw and cooked

foods are now available. When practicable, however, it is preferable to weigh the foods before cooking, since the water content of prepared foods varies considerably, and may be a source of error.

### ii. Exact Work

When testing *total metabolism,* either by direct or by indirect calorimetry, it is customary, first, to establish the fundamental *basal metabolism,* that is, the metabolism that goes on at *absolute rest* when *completely fasting,* and, afterward, to study the influence of definite amounts of special foods or other factors upon metabolism.

In every metabolic study that pretends to *accuracy* the food ingested must be exactly weighed, and its chemical constituents determined by exact analyses. Ordinarily it is desirable that, qualitatively, the food shall correspond to the normal needs of the body, and that, quantitatively, the total caloric need shall be met and the relative amounts of protein, carbohydrate and fat shall not depart far from the proportion of a normal diet.

The diet used by Folin in studying the constitution of normal urine is a very convenient one for general metabolic studies (*q. v.*).

The following diet suggested by Brugsch and Schittenhelm has the advantages of simplicity, palatability and easy analysis:

| Food | Amount | Total N | Fat | Carbohydrate | Water |
|---|---|---|---|---|---|
| Milk | 1,500.0 | 7.5 | 45.0 | 67.5 | 1,335.0 |
| Meat | 150.0 | 5.1 | 1.32 | ..... | 114.0 |
| White bread | 350.0 | 4.48 | 3.5 | 210.0 | 90.0 |
| Butter | 50.0 | 0.1 | 45.0 | ..... | 5.0 |
| One egg | 40.0 | 0.9 | 4.4 | ..... | 30.0 |
| Seltzer water | 500.0 | .... | .... | ..... | 500.0 |

This diet contains:

| | | | | |
|---|---|---|---|---|
| 18.08 × 6.25 = | 113 | *g.* Protein | (×4.1) = | 463.3 Cal. |
| | 99.22 | *g.* Fat | (× 9.3) = | 922.75 Cal. |
| | 277.5 | *g.* Carbohydrate | (× 4.1) = | 1,137.75 Cal. |
| | 2,074.0 | *g.* Water | | |
| | | | | 2,523.8 Cal. |

The diet can easily be varied by adding vegetables and fruit, or by diminishing the amounts of milk, meat, and bread. Obviously, the less modification, the easier the analyses!

Much use can be made of canned milk, jellies, and marmalades, and of certain purchasable powders (dried milk powder; dried vegetable powder; powdered proteins) in metabolic studies, for they are palatable and possess the advantage of constant composition so that a single analysis suffices.

The amount of water taken daily should be nearly constant (2–2½ *l.*).

In studying the *partial functions of metabolism,* the diet will be especially arranged as regards its constituents in the special substance under study, or its forerunners. Thus, in studying *carbohydrate metabolism,* the diet may at first be carbohydrate-free, and, later, definite amounts of carbohydrate of the same sort, or of different sorts, may be added. (See Tests of Carbohydrate Tolerance in Diabetes Mellitus.) In studying the *endogenous purin metabolism,* the diet should be free from purins and their antecedents (nucleic acid, etc.), so as to rule out an exogenous source for purins. (See Purin-free Diet.)

### (*b*) *Analysis of the Foods Ingested*

To save labor, sufficient food of uniform composition may often be prepared ahead of time for the period of metabolic study. It should be kept under conditions that prevent evaporation and decomposition. An aliquot portion may be analyzed, and the amount ingested daily recorded. Meat, bread, butter, and the dried powders may be analyzed in this way. Milk is so variable in its content in protein and fat that daily analyses are desirable, unless canned evaporated milk or milk powder of constant composition be used. Eggs are weighed and the weight of the shell subtracted. Of the net weight, 10.9 per cent is fat and 2.19 per cent nitrogen. Analyses of eggs are time-consuming; in the most exact metabolic studies, in which all foods are accurately analyzed, it is best to avoid the use of eggs.

In analyzing a food chemically we determine its total N-content, and multiply this by 6.25 to get the content in *protein.* Extracting with ether in a Soxhlet apparatus, and evaporating the ether, we get the content in *fat.* Desiccating a weighed portion to constant dry weight, we get the *total solids* and the content in *water.* Charring a weighed portion in a platinum crucible with a known quantity of NaOH; extracting with water and filtering on an ash-free filter; evaporating the filtrate to dryness, we get the *soluble ash;* incinerating the filter and residue, we get the *insoluble ash;* adding the two, we have the content in *inorganic substances.* Hydrolyzing 2-3 grams of the substance by boiling with 2 per cent HCl for 2 hours with a reflux condenser, we convert all the *carbohydrate* into soluble sugar, and can determine the quantity with Fehling's solution or by polarization.

When making studies of *purin metabolism,* or of *mineral metabolism,* the food intake must be analyzed with especial reference to its contents in purin and in the various mineral substances (Ca, Mg, K, Na, P, Cl, etc.).

In studies of *total metabolism* it may sometimes be desirable to make an *elementary analysis* of the food for C, H, and N, and to determine the caloric value precisely by means of a *bomb calorimeter* (Berthelot).

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## (c) *Tables Illustrating the Composition of Ordinary Foods*[1]

TABLE I

### Chemical Composition of Uncooked Food

| I. Animal Foods | Water | Nitrogen | Protein | Fat | Carbohydrate | Cellulose | Ash | Cal. |
|---|---|---|---|---|---|---|---|---|
| Beef (lean) | 75.9 | 3.4 | 21.3 | 0.9 | .... | .... | 1.30 | 98 |
| Beef (fat) | 74.5 | 3.5 | 21.9 | 5.0 | .... | .... | 1.30 | 136 |
| Beef (very fat) | 53.0 | 2.7 | 16.8 | 29.3 | .... | .... | 1.33 | 341 |
| Veal (lean) | 78.8 | 3.1 | 19.4 | 0.8 | .... | .... | 1.33 | 85 |
| Veal (fat) | 72.3 | 3.0 | 18.8 | 7.4 | .... | .... | 1.33 | 146 |
| Mutton (lean) | 76.7 | 3.1 | 19.2 | 2.8 | .... | .... | 0.99 | 105 |
| Mutton (fat) | 53.3 | 2.7 | 16.6 | 28.6 | .... | .... | 0.99 | 334 |
| Pork (lean) | 76.2 | 3.2 | 20.0 | 4.7 | .... | .... | 1.10 | 125 |
| Pork (fat) | 47.4 | 2.2 | 14.5 | 37.3 | .... | .... | 1.12 | 406 |
| Hen's eggs (whole) | 73.67 | 2.1 | 12.55 | 12.11 | 0.55 | .... | 1.12 | 166 |
| Egg albumen | 85.50 | 2.1 | 12.87 | 0.25 | 0.77 | .... | 0.61 | 58 |
| Yolk of egg | 51.03 | 2.6 | 16.12 | 31.39 | 0.48 | .... | 1.01 | 360 |
| One egg (45 *g.*) | 33.2 | 0.9 | 5.65 | 5.45 | 0.25 | .... | 0.5 | 75 |
| Yolk of 1 egg (16 *g.*) | 8.2 | 0.4 | 2.58 | 5.02 | 0.08 | .... | 0.2 | 58 |
| Milk | 88.2 | 0.5 | 3.0 | 3.55 | 4.51 | .... | 0.70 | 65 |
| Cream | 68.82 | 0.62 | 3.76 | 22.66 | 4.23 | .... | 0.53 | 243 |
| Butter | 13.59 | 0.01 | 0.74 | 84.39 | 0.5 | .... | 0.66 | 790 |
| Cream cheese | 30.66 | 0.45 | 2.84 | 62.99 | 2.03 | .... | 1.15 | 606 |
| Swiss cheese | 34.67 | 3.8 | 23.72 | 32.54 | 5.02 | .... | 3.85 | 420 |

[1] For more comprehensive lists, see Atwater's article in the Report of the N. Y. Lunacy Commission (1897-1900), Locke's *Food Values,* Friedenwald and Ruhräh's *Diet in Health and in Disease,* Schwenckenbecher's Tabellen, and J. König's *Chemie der menschlichen Nahrungs- und Genussmittel.*

CHEMICAL COMPOSITION OF UNCOOKED FOOD—Continued.

| II. VEGETABLE FOODS | Water | Nitrogen | Protein | Fat | Carbohydrate | Cellulose | Ash | Cal. |
|---|---|---|---|---|---|---|---|---|
| Boiled rice | 12.58 | 1.0 | 6.73 | 0.88 | 78.84 | 0.51 | 0.82 | 357 |
| Wheat flour | 13.37 | 1.6 | 10.21 | 0.94 | 74.71 | 0.29 | 0.48 | 357 |
| Rye flour | 13.71 | 1.8 | 11.57 | 2.8 | 69.61 | 1.59 | 1.44 | 352 |
| Macaroni | 11.90 | 1.85 | 11.58 | 0.60 | 75.21 | 0.26 | 0.45 | 361 |
| Potatoes | 74.98 | 0.3 | 2.08 | 0.15 | 21.01 | 0.69 | 1.09 | 96 |
| Carrots and turnips | 86.79 | 0.2 | 1.23 | 0.30 | 9.17 | 1.49 | 1.02 | 45 |
| Asparagus | 93.75 | 0.3 | 1.79 | 0.25 | 2.63 | 1.04 | 0.54 | 20 |
| String beans | 88.75 | 0.4 | 2.72 | 0.14 | 6.60 | 1.18 | 0.61 | 39 |
| Cauliflower | 90.89 | 0.4 | 2.48 | 0.34 | 4.55 | 0.91 | 0.83 | 32 |
| Cabbage | 89.09 | 0.5 | 3.31 | 0.71 | 6.02 | 1.23 | 1.64 | 45 |
| Spinach | 88.47 | 0.5 | 3.39 | 0.58 | 4.44 | 0.93 | 2.09 | 38 |
| Lettuce | 94.33 | 0.2 | 1.41 | 0.31 | 2.19 | 0.73 | 1.03 | 18 |
| Apples | 84.79 | 0.06 | 0.36 | .... | 12.03 | 1.51 | 0.49 | 51 |
| Pears | 83.03 | 0.06 | 0.36 | .... | 11.80 | 4.30 | 0.31 | 50 |
| Plums | 81.18 | 0.12 | 0.78 | .... | 11.07 | 5.41 | 0.71 | 52 |
| Grapes | 78.17 | 0.09 | 0.59 | .... | 16.32 | 3.60 | 0.53 | 69 |
| Strawberries | 87.66 | 0.09 | 0.54 | .... | 7.74 | 2.32 | 0.81 | 34 |
| Oranges (without peel and seeds) | 89.01 | 0.12 | 0.73 | .... | 5.54 | 1.79 | 0.49 | 26 |
| Bananas | 76.5 | 0.15 | 0.9 | .... | 21.1 | 0.2 | 1.1 | 102 |

## Composition of Foods Ready for the Table (Schwenckenbecher)

| Foods | Protein | Fat | Carbohydrate | Calories |
|---|---|---|---|---|
| Beef (lean) | 36.6 | 2.8 | ..... | 176 |
| Veal | 26.4 | 1.1 | ..... | 118 |
| Mutton | 30.9 | 4.5 | ..... | 168 |
| Pork | 28.5 | 6.8 | ..... | 180 |
| Chicken | 30.7 | 4.5 | ..... | 168 |
| Roast beef | 26.4 | 2.0 | ..... | 127 |
| Beefsteak | 24.7 | 1.8 | ..... | 118 |
| Roast veal | 30.4 | 6.6 | ..... | 186 |
| Roast mutton | 27.0 | 4.0 | ..... | 148 |
| Roast pork | 35.0 | 8.2 | ..... | 220 |
| Boiled smoked ham | 25.1 | 8.1 | ..... | 178 |
| Bacon | .... | 95.6 | ..... | 889 |
| Oatmeal | 2.2 | 1.5 | 10.4 | 66 |
| Mashed potato | 3.0 | 0.8 | 21.3 | 107 |
| White bread | 7.06 | 0.46 | 56.58 | 265 |
| Zwieback | 8.55 | 0.98 | 75.10 | 352 |
| Soda biscuit | 11.93 | 7.47 | 68.67 | 400 |
| Boiled potatoes | 2.1 | 0.1 | 21.0 | 96 |
| Carrots | 1.1 | 3.2 | 7.0 | 63 |
| Boiled asparagus | 2.0 | 0.3 | 1.3 | 18 |
| Spinach | 3.9 | 2.4 | 1.6 | 45 |
| Sauerkraut | 0.9 | 3.7 | 7.6 | 69 |
| Lettuce salad | 0.7 | 0.5 | 2.1 | 16 |
| Apple sauce | 0.4 | ... | 13.0 | 55 |
| Lump sugar | ... | ... | 99.75 | 410 |
| Honey | ... | ... | 75.0 | 307 |
| Chocolate | 6.18 | 21.0 | 67.7 | 498 |

### Alcoholic Beverages

| | Percentage of Alcohol | Extractives | Dextrin and Sugar | Calories | |
|---|---|---|---|---|---|
| | | | | 1 *g.* Alcohol = 7 Calories | 1 *g.* Alcohol = 0 Calories |
| Pilsener beer | 4.36 | 4.67 | 3.2 | 50 | 19 |
| Moselle wine | 7.66 | 2.21 | .... | 63 | 9 |
| Rhine wine | 10.16 | 2.57 | .... | 82 | 10 |
| Claret | 7.8 | 2.56 | 0.3–1.7 | 65 | 10 |
| Champagne | 10.2 | 14.0 | 12.10 | 129 | 57 |
| Port wine | 16.6 | 8.05 | 5.82 | 149 | 33 |
| Brandy | 42.0 | 1.0 | 0.7 | 298 | 4 |

TABLE II

### Chlorid Content of Various Foods, Calculated as NaCl (Strauss)

1. Raw Foods

| Foods | Per Cent of NaCl |
|---|---|
| Milk | 0.15–0.18 |
| Unsalted butter | 0.02 |
| Salted butter | 1.0 |
| Cheese | 1.5–2.5 |
| Egg: Whole egg | 0.14 |
| White of egg | 0.19 |
| Yolk of egg | 0.02 |
| Caviar | 6–7 |
| Meat | 0.1 |
| Cereals | 0.01–0.1 |
| Most vegetables | 0.1 |
| Spinach | 0.21 |
| Fruits usually less than | 0.06 |

2. Foods Ready for Eating

| Foods | NaCl In 100 *g.* | NaCl In a Single Portion |
|---|---|---|
| Bouillon | 0.55–1.0 | ..... |
| Soups | 0.34–0.90 | ..... |
| Roast beef } Veal cutlet } | ..... | 1.9–2.8 |
| Beefsteak | ..... | 3.0 |
| White bread | 0.48–0.70 | ..... |
| Vegetables (mashed potato; cauliflower) | ..... | 0.6–0.9 |
| Asparagus | ..... | 2.7–3.5 |

TABLE III

## Purin Content of Various Foods

PURIN CONTENT OF MEATS AND FISH (WALKER HALL)

| | Percentage of Purin Nitrogen | Average Percentage of Nitrogen | Calculated as Purin Bodies | Undried as Grams per Kilo. | Purins as Grains per Pound |
|---|---|---|---|---|---|
| Cod | 0.0219 | 0.0233 | 0.0582 | 0.582 | 4.074 |
| Plaice | 0.0334 | 0.0318 | 0.0795 | 0.795 | 5.565 |
| Halibut | 0.0405 | 0.0408 | 0.1020 | 1.020 | 7.140 |
| Salmon | 0.0482 | 0.0466 | 0.1165 | 1.165 | 8.155 |
| Tripe | 0.0235 | 0.229 | 0.0572 | 0.572 | 4.007 |
| Australian mutton | 0.0365 | 0.0386 | 0.0965 | 0.965 | 6.755 |
| English mutton | 0.0411 | ..... | ..... | ..... | ..... |
| Loin of veal | 0.0454 | 0.0465 | 0.1162 | 1.162 | 8.137 |
| Neck of veal | 0.0300 | ..... | ..... | ..... | ..... |
| Loin of pork | 0.0485 | 0.0485 | 0.1212 | 1.212 | 8.487 |
| Neck of pork | 0.0257 | 0.0227 | 0.0567 | 0.567 | 3.967 |
| Ham | 0.0505 | 0.0492 | 0.1155 | 1.155 | 8.085 |
| Ham fat | 0.0419 | ..... | ..... | ..... | ..... |
| Ribs of beef | 0.0455 | 0.0455 | 0.1137 | 1.137 | 7.959 |
| Sirloin of beef | 0.0506 | 0.0522 | 0.1305 | 1.305 | 9.135 |
| Steak | 0.0826 | 0.0826 | 0.2065 | 2.066 | 14.455 |
| Liver | 0.1125 | 0.1101 | 0.2752 | 2.752 | 19.264 |
| Thymus (sweetbread) | 0.4025 | 0.4025 | 1.0063 | 10.063 | 70.431 |
| Chicken | 0.0456 | 0.0518 | 0.1295 | 1.295 | 9.065 |
| Turkey | 0.0504 | 0.0504 | 0.1260 | 1.260 | 8.820 |
| Rabbit | 0.0305 | 0.0380 | 0.0970 | 0.970 | 6.314 |

PURIN CONTENT OF BREAD, CEREALS AND VEGETABLES

| | Percentage of Purin Nitrogen | Percentage Calculated as Purin Bodies | Grams per Kilo. | Grains per Pound |
|---|---|---|---|---|
| White bread | No trace | | | |
| Oatmeal | 0.0212 | 0.0530 | 0.530 | 3.4563 |
| Rice | No trace | | | |
| Pea meal | 0.0156 | 0.0390 | 0.390 | 2.5413 |
| Beans (haricot) | 0.0250 | 0.0637 | 0.6375 | 4.1661 |
| Lentils | 0.0250 | 0.0637 | 0.6375 | 4.1661 |
| Lentils (malted) | 0.0150 | 0.0375 | 0.3755 | 2.3340 |
| Potatoes | 0.0008 | 0.0020 | 0.0200 | 0.1400 |
| Onions | 0.0031 | 0.0090 | 0.090 | 0.0630 |
| Tapioca | No trace | | | |
| Cabbage | " " | | | |
| Lettuce | " " | | | |
| Cauliflower | | | | |
| Asparagus (cooked) | 0.0086 | 0.0215 | 0.215 | 1.5050 |

PURIN CONTENT OF BEVERAGES

| | Purin Bodies (Grains per Pint) | | Purin Bodies (Grams per Liter) |
|---|---|---|---|
| Tea | 1.2 | Lager beer | 0.125 |
| Coffee | 1.7 | Pale ale | 0.145 |
| Chocolate | 0.7 | Porter | 0.155 |
| Cocoa | 1.0 | | |

TABLE IV

**Loss of Food Substances in the Feces of Normal Persons (Rubner)**

| | Percentage of Total Dry Substance Lost | Percentage of Protein Lost | Percentage of Fat Lost | Percentage of Carbohydrate Lost |
|---|---|---|---|---|
| Roast meat | 5.3 | 2.6 | 19.2 | .... |
| Boiled and roast meat | 4.9 | 2.0 | .... | .... |
| Hard-boiled eggs | 5.2 | 2.6 | 4.4 | .... |
| Milk | 8.8 | 7.1 | 5.3 | 10.0 |
| Cheese | 6.4 | 3.3 | 5.2 | .... |
| White bread | 4.2 | 21.8 | .... | 1.1 |
| Rye Bread | 31.1 | 36.7 | .... | 7.9 |
| Pumpernickel | 19.3 | 43.0 | .... | 13.8 |
| Protein poor macaroni | 4.3 | 17.1 | .... | 1.2 |
| Protein rich macaroni | 5.7 | 11.2 | .... | 2.3 |
| Rice | 4.1 | 20.4 | .... | 0.9 |
| Corn-meal | 6.7 | 15.5 | .... | 3.2 |
| Peas | 9.1 | 17.5 | .... | 3.6 |
| Boiled and baked beans | 18.3 | 30.2 | .... | .... |
| String beans | 15.0 | .... | .... | .... |
| Potatoes | 9.4 | 30.5 | .... | 7.4 |
| Cabbage | 19.4 | 18.5 | .... | 15.4 |
| Yellow turnips | 20.7 | 39.0 | .... | 18.2 |
| Mixed diet (average loss) | .... | 8.0 | 5.0 | 3.0 |

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## 3. The Collections of Excretions and Their Analysis

### (*a*) *Collection of the Urine*

The urine for each 24 hours is kept by itself, being collected in a 3 *l.* vessel containing a few crystals of thymol (as disinfectant), or, better, 10-20 c.c. toluol. The urine may be passed directly into the vessel, or it may be collected *quantitatively* and transferred to it after each voiding.

The 24-hour period may extend from 8 a. m., to 8 a. m. Just before beginning the first period, urine is voided and discarded. At the end of each 24-hour period urine is voided and added to the urine of the period. Breakfast should not be taken until the new 24-hour period begins. On defecation, no urine should be lost. An aliquot portion of the well-mixed 24-hour urine can be kept in a well-stoppered bottle (thymol preservation) for many chemical studies. If the urine is alkaline, it should be rendered slightly acid with HCl (known quantity). If ammonia or acetone determinations are to be made, fresh urine should always be employed.

### (*b*) *Analyses of the Urine*

The total urine for each 24 hours is exactly measured with a graduate and the amount recorded. After the urine has been well mixed, the specific gravity is taken. For the total N determination by Kjeldahl's method, 5 c.c., exactly measured with a calibrated pipet, will suffice. For the determination of carbon, a small portion is measured in a pipet, carefully transferred to a "boat" and dried over $H_2SO_4$ in vacuo at the room temperature. The elementary analysis is made with the dried residue.

### (*c*) *Collection of the Feces*

In collecting feces, the patient should be told first to urinate, in order that there shall be no mixing of urine and feces. In order to *mark the beginning of the period* to be studied, one gives three tablespoonsful of a charcoal mixture (Carbo ligni 15.0; Mucilago acaciae 15.0; Aq. menth. pip. 60.0), or 0.3-0.5 g. carmin in tablet form, on an empty stomach, the first thing in the morning, no food having been taken during the preceding 12 hours. If the charcoal mixture be used, the mouth should be thoroughly rinsed out afterwards.

In the afternoon of the first day, the bowels should be emptied, using a glycerin suppository or an enema if necessary. The feces obtained will not contain charcoal (or carmin), and should be discarded. At the next stool, the feces will appear diffusely black (or red) when passed, and only a few unstained particles will need to be separated from the general mass and discarded.

The feces must be collected for the whole period of the study (three to eight days). On the morning *ending the last* 24 *hours of the period* of metabolic study, charcoal or carmin should be given again; the next feces containing the marking substance does not belong to the study and should be discarded.

The *total feces for the period* are mixed in an evaporating dish with a measured amount of 5 per cent oxalic acid solution (or, if preferred, of a ½ per cent solution of $H_2SO_4$), evaporated to dryness on a water bath, desiccated in a drying chamber, weighed, finely powdered, and thoroughly mixed and kept for chemical

analysis. The weight of the fresh feces, less the weight of the acid solution and of the dried residue will be the weight of the water in the feces for the period.

### (*d*) *Analyses of the Feces*

The N-content is determined by Kjeldahl's method, the C-content and the H-content by Liebig's method.

To determine the fat-content, an ether extract is made of an aliquot portion (say 2 g.) by means of a Soxhlet apparatus. Afterwards, the soaps present can be converted into fatty acids by boiling the contents of the Soxhlet thimble in 1 per cent alcoholic solution of HCl, and the fatty acids extracted with ether or petrol-ether in a Soxhlet apparatus.

To determine the carbohydrate content, an aliquot portion of dried feces is boiled in a reflux condenser, with a 2 per cent solution of HCl, for several hours (until hydrolyzed), after which the sugar content is quantitatively determined by a copper reduction method. (See Quantitative Determination of Sugar in Urine, Part IX.)

The ash is analyzed in the same way as advised for the ash of the urine. (See above.)

### (*e*) *Collection and Analysis of Other Materials*

In exact metabolic studies, it may be necessary to collect, and to analyze, the *sweat,* the *vomitus,* the *milk,* the *sputum,* and the *menstrual blood.* Such studies complicate a metabolic investigation, and should be avoided unless absolutely necessary. The loss through *hair, nails,* and *epidermis* is so slight as to be negligible.

## 4. The Organization of a Metabolic Study

### (*a*) *Preparation*

The whole study should be first thoroughly planned and outlined. The precise object of the study should be clearly in mind, and everything directed to obtaining it, avoiding, of course, all unnecessary work, but making sure that all conditions necessary for the accurate prosecution of the study designed are complied with.

The special diet to be used during the period proper should be used also for at least the three preceding days, in order that the patient's body may adjust itself to the new conditions and his metabolism become "even." In studies of protein metabolism especially this preliminary adjustment is essential if gross errors are to be avoided.

### (*b*) *The Period of Study*

A metabolic study of at least 3 or 4 days (except in studies of total metabolism) is essential if results of value are to be obtained. Daily variations are so great that it is necessary to observe a period of days (See Collection of Urine and Feces), and take the *average* daily change.

When studying the influence of a given factor on metabolism, the period of study should be divided into three subperiods: (1) a *preliminary period,* during which the ordinary metabolism is observed; (2) a *main period,* during which the factor whose influence is to be studied is in operation, and (3) an *after-period,* during which the duration of the effect is determined. Each subperiod should consist of several days.

In *calorimetry,* the total metabolism is determined in the middle of a period of study. It may be determined for 24 hours or longer by means of a large calorimeter like that at Benedict's disposal in the Carnegie Institution for the Study of Nutrition, in Boston, or, for a shorter time, with less expensive apparatus.

In *indirect calorimetry* the total metabolism may be followed for a brief period with the aid of the Zuntz-Geppert apparatus.

### (c) *The Balance*

By contrasting the intake with the output, the **balance** for a given substance is obtained. We determine whether (1) the intake and output are equal (= *equilibrium*), (2) the intake exceeds the output (= *positive balance*), or (3) the output exceeds the intake (= *negative balance*).

According to the special indication for the metabolic study, we examine the nitrogen balance, the exogenous purin balance, the chlorin balance, etc.

### (d) *Metabolic Studies on Animals*

Important as these are for the advance of knowledge of metabolism, it would take us too far afield to attempt to discuss them here. A good epitome will be found in Brugsch and Schittenhelm's text-book.

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## 5. Tests of Assimilation

*(Digestion and Absorption)*

An analysis of the food ingested and of the feces excreted will suffice for the determination of the patient's power of digestion and absorption; or, in other words, of utilizing the food ingested.

The method has its limitations, since the feces contain not only undigested or unabsorbed foodstuffs, but also residues of the digestive secretions, epithelia and bacteria.

In *diseased states* the food may be imperfectly digested, imperfectly absorbed, or both, and it may be desirable to test the patient by giving him a diet that ordinarily can be easily digested and absorbed and find out how much of it he is able to utilize.

As a **diet** suitable for such a test, von Noorden advises the following:

Milk, 1000 *c.c.*; white bread, 180 *g.*; tender beef, 200 *g.*; butter, 70 *g.*; water, wine, and salt as desired. The diet should be given for 2-3 days, and the feces marked, collected, and analyzed.

Normally, about 5-6 per cent of the dry residue of this diet, 6 per cent of the total N, and 5-8 per cent of the fat are lost in the feces.

When a line on the *fat metabolism* only is desired, the following diet is satisfactory and is simpler to analyze:

Milk, 2-3 *l.*; butter, 50-100 *g.*; white bread, 100-200 *g.*

This diet is given for 2-4 days. The feces are marked, collected, and analyzed. Normally, the loss through the feces is 5-10 per cent of the dry substance of the diet, 5-10 per cent of the total N, and 5-10 per cent of the fat.

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## 6. Determinations of Protein and Nitrogen Metabolism

Many of the studies of the subject reported in the bibliography are utterly worthless.

It is not safe to calculate the protein-content of foods from tables. It is necessary to make exact determinations of the total nitrogen by Kjeldahl's method and from them to calculate the protein-content. The patient should be kept in caloric equilibrium during the period of study. A preliminary period of *adjustment* to the diet (*q. v.*) is essential in studies of protein metabolism. Finally, a rather *long period* (several weeks) of observation is necessary if sources of error are to be ruled out. Studies of protein metabolism of short duration are rarely of any value.

The **nitrogen balance** is calculated by the methods already described. From it, it is easy to calculate how much, if any, of the patient's own protein, or his own muscle, has been lost, or gained, during the period of the experiment, since 1 g. of N corresponds to 6.25 g. of protein and to 29.4 g. of muscle substance.

Formerly *urea determinations* were used for gaining a clue to the protein metabolism. Now that Kjeldahl's apparatus is in such universal

use systematic urea determinations for this purpose are rarely necessary. Urea determinations, however, are still of value for some studies (See Ambard's Coefficient, etc.).

It will be found convenient in studying the nitrogen metabolism to use a *diet* in which the protein content is fairly constant. Among such foods may be mentioned milk, lean meat, eggs, bread, and rice (See Arrangement of Diet).

In case of **nitrogen retention** ( = positive N-balance), we may give large quantities of *water* to see whether a part of the retained nitrogen can be "washed out." We may also follow the *phosphorus* and the *sulphur balance,* and determine whether these substances are retained in the proportions in which they occur in the protein of the body ($N : P_2O_5 = 6 : 1$; and $N : S = 16 : 1$). It goes without saying that the *body weight* should be exactly recorded at the same time each day in the course of every study of metabolism.

The time for superficial studies of protein metabolism has long since passed. Energy thus spent is utterly wasted. From now on, only exactly controlled studies that will stand the strictest criticism can be considered worth while.

## 7. Determinations of Nuclein and of Purin Metabolism

### (*a*) *Introduction*

The purin-content of the urine consists chiefly of combined and free uric acid; purin bases are also present in small amounts. Normally the uric-acid content is to the purin-bases content as 10:1.

The sources of the purins of the urine have already been described (see above). To recapitulate, they are:

1. **Exogenous,** from (a) the nucleic acids (animal and vegetable) of the food and (b) the extranuclear purin compounds of the food (guanylic acid in glands; inosinic acid in meat; hypoxanthin in meat; methyl purins in tea, coffee, cocoa or in drugs like diuretin, theocin, caffein, coca-cola, etc.).
2. **Endogenous,** from (a) the animal nucleic acid of the *nuclear metabolism* of the body cells (b) the *metabolism of the extranuclear purin-compounds* in the tissues (guanylic acid in the glands; inosinic acid and hypoxanthin in the muscles.

We first determine the *endogenous uric acid* (or *endogenous total purin*) output—that is, the output on a purin-free diet—and, afterwards, the degree and rate of excretion of *exogenous purins,* using either a mixed diet, the purin-content of which is determined by analysis; or, better still, a purin-free diet plus a definite amount of pure thymus nucleic acid, or pure yeast nucleic acid (analyzed for its purin-content).

### (*b*) *Purin-free Test Diet*

*Breakfast.*—Fruit, 250 *g.*; milk, 250 *c.c.*; one roll.

*Dinner.*—Pudding (consisting of 100 *g.* wheat flour, 150 *c.c.* milk, 3 eggs, and 50 *g.* butter); 200 *g.* stewed fruit.

*Supper.*—Cereal (consisting of 50 *g.* meal, 750 *c.c.* milk, 20 *g.* sugar); fruit (raw or stewed), 250 *g.*; one roll; butter, 50 *g.*

During the day a liter of water should be taken in addition to the fluids of the above diet.

### (*c*) *Determination of the Metabolism of Endogenous Purins*

We study: 1. the output of endogenous purins in the urine after the patient has been, for at least three days preceding the collection of urine for the determination, on a purin-free diet; and 2. the content of the blood in endogenous purins after a similar period of purin-free diet (for methods of examination of the blood and urine, see Parts VII and IX). A series of determinations should be made, and the average taken as the endogenous value.

### (*d*) *Determination of the Metabolism of Exogenous Purins*

After the content of the blood and the urine in endogenous purins (fairly constant for each person) has been determined, we study the capacity of the body to absorb, transform and excrete exogenous purins. Formerly a meal of sweetbreads, or of meat, was given, and the excretion of exogenous purins followed. It is far better to add to a purin-free diet a definite quantity of pure nucleic acid; say, 5 or 6 grams in 24 hours.

For at least three or four days preceding the nucleic acid intake the patient is kept on a purin-free diet. Nucleic acid is added to the purin-free diet for three or four days, and then the purin-free diet is returned to, and maintained, until the purin output in the urine has again reached the person's constant endogenous level. During all three periods we follow (1) the total N-intake, (2) the total $P_2O_5$ intake, (3) the total N-output in urine and feces, (4) the total $P_2O_5$ output in urine and feces, and (5) (during the administration of nucleic acid and the after-period) the uric acid output and the purin base output in both urine and feces.

It may be of interest to make one set of experiments with thymus nucleic acid and another with yeast nucleic acid.

In experiments on animals, it is necessary to follow the *allantoin* output, since, in them, uric acid is transformed to allantoin. This does not occur in man.

It is also of interest to follow the glycocoll output, since the curves of glycocoll and uric acid sometimes run in opposite directions (Umber).

Normal persons catabolize nucleic acid and excrete the purins derived from it promptly. In *gout* the excretion may be greatly delayed. The purin excretion before, during and after an attack of gout exhibits some other remarkable features (See Gout).

In addition to determinations following ingestion of nucleic acid, we may, if we wish, make determinations after the ingestion of (1) guanylic acid (2) inosinic acid, (3) adenin, (4) guanin, (5) hypoxanthin, (6) xanthin, or (7) uric acid. As yet, however, very little testing of this sort has been done with the use of the newer methods. (See also Gout.)

## 8. Determinations of the Carbohydrate and of the Fat Metabolism

### (*a*) *Introduction*

Here we have to depend chiefly on the results of studies of total metabolism (See below), though studies of partial metabolism are also helpful. Normally the *end-products* of the metabolism of both carbohydrates and fats are $CO_2$ and $H_2O$, the former being excreted chiefly in the expired air. Tests of assimilation show how much carbohydrate and fat undergo absorption, but give no clue to the amount catabolized, since the absorbed portions may be (1) catabolized, (2) stored up as glycogen or fat, or (3) in part excreted as sugar (in diabetes mellitus).

Studies of *total metabolism,* especially of the resting-fasting or basal metabolism, will show us (1) how active the oxidative processes are (the flame burns low in endogenous obesity), and (2) what substances are burned (carbohydrate, fat, or protein), and their relative proportions.

### (*b*) *Studies of Carbohydrate Tolerance*

Even when there is no spontaneous glycosuria it may be desirable to test the capacity of the body to ingest carbohydrate without the appearance of glycosuria. Thus the normal person, if he ingest at one time a large amount of glucose, will develop a transitory glycosuria (so-called **alimentary glycosuria,** or **glycosuria e saccharo).** Such an alimentary glycosuria cannot be produced in healthy people by the ingestion of starch, for the assimilation of this occurs gradually, not suddenly. In beginning diabetes mellitus, however, 100 g. bread taken in the morning may cause glycosuria (so-called *glycosuria ex amylo*). But with glucose, galactose, and saccharose an alimentary glycosuria easily occurs, and with lactose and levulose an *alimentary lactosuria* and *alimentary levulosuria* can be produced, though less easily than a glycosuria with glucose.

The *tolerance* in health varies somewhat. As a rule, a healthy per-

son who takes on an empty stomach in the morning 100 g. glucose dissolved in tea will show in the urine passed during the next three hours a trace or even a few grams of glucose. If the tolerance is lower, so that 60-80 g. glucose cause *glycosuria e saccharo,* one will suspect a deviation from the normal, namely, an inability normally to catabolize glucose; we then test also for *glycosuria ex amylo* (see above).

Tests for *alimentary galactosuria* and for *alimentary levulosuria* have been used as a measure of hepatic function (*q. v.*).

In **diabetes mellitus,** there is spontaneous glycosuria on an ordinary diet. In the *mild cases* there is some carbohydrate tolerance, though this is lower than normal. It can be determined exactly (See Diabetes Mellitus). In *severe cases* of diabetes there is no tolerance whatever for carbohydrates, all carbohydrate ingested being excreted as sugar. Indeed, in such cases the organism may make sugar out of ingested protein or out of body protein, possibly also out of fat!

When the tolerance for carbohydrate is low, the body may be able to tolerate *some forms of carbohydrate* (oatmeal, potato, etc.) better than other forms (bread), and this can be determined by special tests.

In severe diabetes, where sugar is made from the proteins of the food, some forms of protein may increase the glycosuria more than others. Thus Lüthje found, in severe human diabetes, that casein and pancreas sweetbreads increase the glycosuria more than beef, egg albumen and thymus sweetbreads, while in experimental phlorhizin diabetes, J. T. Halsey discovered that casein causes less sugar excretion than egg albumen. In human diabetes, egg albumen seems least harmful, while plant protein, casein, and meat proteins are harmful in an ascending scale (von Noorden).

### (c) *The D:N Ratio*

Lüthje was the first to prove in experimental pancreatic diabetes that the sugar excreted could not all be derived from carbohydrate. Minkowski asserted that in experimental pancreatic diabetes, the relation of dextrose to nitrogen excreted (so-called **D:N ratio**) is constant, namely 1:2.8, and concluded that, for every 100 g. protein broken down, 45 g. sugar could be formed; he believed that this constant ratio was reached only when a maximal amount of sugar was being made from protein.

Since then, considerable interest has attached to the determination of the D:N ratio in human diabetes. It was soon found, however, that the ratio may be much higher than 1:2.8; thus Rumpf studied a case in which 40 g. of protein only was metabolized, but the sugar output was 77 g. In phlorhizin diabetes, Lusk at first thought that a constant relation existed between the sugar excreted and the protein metabolized, but modified this view later.

Friedrich Müller found that when the D:N ratio is low, there is often a nitrogen retention difficult to explain; later, the view became prevalent that this can be explained by a partial degradation of protein, a part of it going to form sugar, the sugar free part being utilized for protein syntheses.

### (*d*) *The Oxyacids, the Keto-acids and the Ketones in Acidosis*

The **acetone bodies** (*acetone* or dimethylketone; *diacetic acid* or aceto-acetic acid; and the *l*-form of *beta-oxybutyric acid*) have already been referred to as occurring in the blood and urine in diabetes mellitus and in certain other conditions (*e. g.,* inanition; cyclical vomiting of children). These substances are not present in normal urine. Diacetic acid is probably a normal intermediary product in the metabolism of fats (*q. v.*).

To throw light upon an **acidosis,** a quantitative study of these bodies is often clinically necessary. As much acetone as 19 *g.* per day has been found in the urine, and no less than 3.6 *g.* was excreted in the breath in a case reported by Schwarz. Amounts of beta-oxybutyric acid exceeding 100-150 *g.* per day have been excreted in the urine in diabetes (Naunyn, Magnus-Levy).

For the methods of determination of these substances, see Part IX (Examination of the Urine).

In certain instances it may be desirable to test the *capacity of the body to oxidize diacetic acid and beta-oxybutyrate of soda* given by the mouth. In other instances the *ketogenous,* or the *antiketogenous, effect* of administration of certain subtsances (amino-acids, fatty acids, carbohydrates) may be followed.

Light may also be thrown upon an acidosis by studies of (1) the *H-ion content* of the blood (*q. v.*), (2) the *$CO_2$-tension* of the expired air (*q. v.*), (3) the *balances of the mineral constituents* (Ca, Mg, K, Na, etc.), and (4) especially the *$NH_3$ content* of the urine. For the relation of these ketone bodies and oxyacids to the deadly coma diabeticum, see Diabetes Mellitus.

Of the metabolism of monobasic oxyacids other than beta-oxybutyric acid, some attention should be paid to that of **d-lactic acid** (= alpha-oxy-propionic acid or $CH_3.CHOH.COOH$), a normal constituent of all organs of the body (especially of the muscles), and of the urine. It probably is related both to carbohydrate and to protein metabolism, since it arises both as an intermediary product in the catabolism of glucose in the body and as a by-product in the deaminization of alanin. Most of what is formed is further catabolized to $CO_2$ and $H_2O$. Lactic acid can be determined by converting it into its characteristic zinc salt.

### (*e*) *Pentoses*

The only pentose entering into constituents of the animal body is, as we have seen, *d-ribose.* It is a normal constituent of guanylic acid and of inosinic acid. The other pentoses that are found sometimes in the urine are (1) *d, l-arabinose,* of unknown origin; (2) *l-xylose,* probably derived from the pentosans of the food (fruits). For the qualitative color reac-

tions, and the quantitative methods of determination of pentoses, see Part IX (Examination of Urine).

### (*f*) *Glycuronic Acid and Glycuronates*

For methods of determination in the urine, see Part IX.

## 9. Determinations of Mineral Metabolism

A consideration of the complexity of the factors governing the normal metabolism of inorganic matter, the variable resorption, the often long delayed elimination, the numerous paths of excretion, should all impress the clinician with the dangers of drawing diagnostic deductions from any but the most complete metabolic investigations. Such researches have as yet been too few in number firmly to establish types of deviation as characteristic of certain disease processes.

The first essential in a study of mineral metabolism is an exact analysis of the **mineral content of the food.** Calculation of this content from tables of values is not permissible, for the variations in mineral content of the same type of food are too great. It is, of course, best to make the diet as simple as possible while furnishing the necessary calories. It is frequently of advantage to study the effects of an *ash-free diet* in certain conditions. Such a diet may consist of the whites of 18 eggs, 120 grams of olive oil and 200 grams of crystallized sugar (Taylor).

Further, analyses of the **mineral excretion** in the urine and feces are required in every case. The sweat must usually be neglected because of technical difficulties. Sputum, however, should be studied when appreciable quantities are produced.

As a rule, the study of the metabolism of only *one* mineral body should be taken up at one time, but because of physiological interrelationships, it will sometimes be advisable to take up the investigation of several of these bodies simultaneously. In the study of a case of pathological ossification, for instance, it would be advisable to study not only the calcium but also the magnesium and phosphorus metabolism (see Rickets and Osteomalacia).

The first period of such an investigation should usually be devoted to determining whether, upon a normal intake, the balance of intake and output is even, positive (*i. e.*, intake > output), or negative (*i. e.*, output > intake). It should also be determined how great an increase or decrease of the intake is needed to establish an equilibrium. It is only by the accumulation of such data from many cases, as carefully controlled as possible, that the present confusion in this field can be cleared up.

For the *chemical methods* employed in the analyses of the food and excreta for mineral constituents, the reader is referred to Part IX and to larger handbooks (See References), concerning the studies of the chlorids in the blood and urine in renal disease, see Part X.

## 10. Determination of the Water-balance

We have already referred to the significance of water in metabolism (Part XIII, Section i, 9).

Exact determinations of water-balance are not easy. It would be ludicrous, if it were not pathetic, to find even hospital physicians thinking that they are following the water-balance when they merely ask a nurse to keep a record of the fluid intake and of the quantity of urine passed! The urine is, of course, only a part, though an important part, of the *total output* of water. In addition, the water-content of (1) the feces, (2) the skin, and (3) the expired air has to be considered. Minor quota are represented by losses through tears, nasal secretion, sputum, menstrual fluid, and sperm.

The *sources of water* in the body include (1) the water of food and drink, and (2) the "oxidation water" arising during metabolism.

**Determinations of the total water-balance** are possible, therefore, only under exceptional conditions, where apparatus is available for collection and measurement of the water output of the skin and breath, as well as of the urine and feces, and where the content of the food and of the excreta can be rigidly controlled by exact chemical methods.

**Partial determinations of water-metabolism** are, therefore, much more common in clinical work than determinations of the balance of total water. Thus the effect of diuretics, of cardiotonic treatment, of water drinking, etc., on the *body weight* and on the *urinary output* can be studied clinically, and with advantage.

## 11. Determinations of Vitamin Metabolism

For the little that is known regarding this new and exceedingly interesting subject the reader should consult the articles by Osborne and Mendel on Growth, and the collective review by C. Funk. (For references, see Part XIII, Section i, A, 10.)

## 12. Determinations of Total Metabolism (Clinical Calorimetry)

Here we make use of (a) Direct Calorimetry and (b) Indirect Calorimetry, and (c) Rough Approximative Methods.

### (*a*) *Direct Calorimetry*

**Definition.**—The determination directly of the heat produced during oxidation by means of a calorimeter.

**Calorimeters.**—For the calorimetry of *foodstuffs, urine, feces,* etc.,

the **bomb-calorimeter** of Berthelot is used. For the results obtained on a great series of foodstuffs, see the treatise of J. König.

For the direct calorimetry of living beings, **calorimeters for animals** are available (Rubner) and even **calorimeters for man** (Atwater and Rosa, Benedict, Tigerstedt). Since, however, these cannot be employed for clinical work except in special research institutions, they will not be described here.

### (*b*) *Indirect Calorimetry*

**Definition.**—The indirect determination of the heat produced during oxidations in the body by calculations based upon oxygen consumption and carbon dioxid excretion (measured by a respiration apparatus), and upon the nitrogen of the intake and the output.

**Forms of Respiration Apparatus.**—Two main types of respiration apparatus are in use: (1) a type designed to permit of following the gas metabolism over longer periods (24 hours or more); and (2) a type designed for following the gas metabolism over short periods (30-60 minutes) only.

#### i. Respiration Apparatus for Longer Periods of Study (24 hours or more)

The patient is placed in a chamber in which he can live and be fairly comfortable for 24 hours or longer, and by means of which his oxygen consumption and his carbon dioxid excretion for the period can be accurately determined. The urine and feces may also be collected quantitatively for analysis. Of apparatus of this type, two varieties are in use (1) that introduced by Pettenkofer and used by him and Voit, and (2) that introduced by Regnault and Reiset.

1. *Apparatus of the Pettenkofer Type (Pettenkofer, Voit, Rubner)*

In this apparatus, the chamber is ventilated by a current of air that passes through it; the entering air and the discharged air of the chamber are analyzed for their $O_2$ and $CO_2$ content, so that the total $CO_2$ production of the patient can be calculated.

2. *Apparatus of the Regnault and Reiset Type (Regnault and Reiset, Atwater and Benedict, Lusk)*

In the apparatus devised by Regnault and Reiset, the patient is placed in a hermetically sealed chamber; oxygen is supplied to him from a tank within the chamber, and the carbon dioxid is absorbed as it is formed.

The new **Universal Respiration Apparatus** of Benedict, though designed especially for briefer periods of study, can also be used for longer periods, at any rate, for children. The system of ventilation in it is so arranged that the patient breathes through a nose piece or a mouth piece. The $CO_2$ and $H_2O$ formed are absorbed.

#### ii. Respiration Apparatus for Brief Periods of Study (30–60 minutes)

Three principal methods are in use: (1) The Zuntz-Geppert Respiration Apparatus; (2) The Head Respiration Apparatus (Jaquet, Grafe) and (3) The Universal Respiration Apparatus of Benedict.

### 1. *The Zuntz-Geppert Apparatus*

**Principle.**—The gas exchange of the lungs only is measured. That of the skin is neglected—not a serious matter, since it does not amount to more than 1 per cent of the total gas exchange, save in exceptional circumstances that can be avoided.

**Technic.**—For the full details of the use of this method, the article by Magnus-Levy should be consulted. The main points only will be mentioned here.

The patient having taken no food during the preceding 12-14 hours, lies comfortably and absolutely quietly, in a warm room in the recumbent position, and breathes (the nose closed) through a mouth piece, so arranged that on inspiration one valve is used, on expiration another, thus permitting of entire separation of the inspired and the expired air. The mouth piece must be fitted air-tight to the mouth; the nose is closed by a clamp. The patient is first allowed to breathe quietly for about half an hour, until he becomes accustomed to the apparatus. The actual experiment then begins and is continued for from fifteen to thirty minutes or longer. The expired air passes through a gas clock and is measured. The apparatus permits of withdrawal of average samples of the expired air for analysis; on making the analysis, the $CO_2$ is absorbed by KOH, and the $O_2$ by phosphorus, and the volume before and after each absorption accurately measured. One thus obtains the percentage of $CO_2$ and of $O_2$ in the sample of expired air, and thus can easily calculate the amount of oxygen taken in and of $CO_2$ given off during the whole period, as well as the amounts per minute. In all gas measurements the calculations are corrected for 0° C. and 760 mm. barometric pressure, and from the data thus obtained the weight of the gases in grams is easily estimated. One liter of oxygen at 0° and 760 weighs 1.430 *g.*; one liter of $CO_2$ under the same conditions weighs 1.966 *g.*

The amount of oxygen used is a direct measure of the heat production in the body. Very different amounts of oxygen are required to burn equal weights of the different food constituents, and the amounts of $CO_2$ produced also differ.

As we have seen (p. 759), starch and fat are completely oxidized in the body to $CO_2$ and $H_2O$, but the protein is not completely burned, some of the constituents of protein going over into the urine and feces in a partially oxidized state. The following table (Magnus-Levy) shows these facts clearly:

| | No. of c.c. of $O_2$ Required to Oxidize | No. of c.c. of $CO_2$ Formed on Oxidation | No. of Calories Developed on Oxidation | No. of Calories Corresponding to 1 c.c. of $O_2$ Used | No. of c.c. of $CO_2$ for each c.c. of $O_2$ Used |
|---|---|---|---|---|---|
| 1 *g.* starch..... | 828.8 | 828.8 | 4.1 | 5.0 | 1.000 |
| 1 *g.* fat..... | 2,019.2 | 1,427.3 | 9.3 | 4.7 | 0.707 |
| 1 *g.* protein..... | 966.1 | 781.7 | 4.1 | 4.6 | 0.808 |

If two patients in a Zuntz-Geppert experiment use up the same amount of oxygen, the heat production must be nearly the same in each; the difference will always be less than 8 per cent. On the other hand, if the two patients produce equal amounts of $CO_2$ during an experiment made under similar conditions, a difference of as much as 30 per cent in heat production would be possible.

The number of c.c. of $CO_2$ produced for each c.c. of oxygen used, that is, the quotient $\frac{CO_2}{O_2}$ is known as the **respiratory quotient.** From the above table it will be observed that this quotient is largest when carbohydrate is burned and smallest when fat is burned. In a given Zuntz-Geppert experiment one can easily tell, therefore, whether carbohydrate or fat is being predominantly burned, since in the resting-fasting condition of the experiment the nitrogen metabolism may be considered as constant. This explains why the respiratory quotient is often low in *diabetes,* since the diabetic patient is giving off a part of his carbohydrate unburned through the urine (glucose, beta-oxybutyric acid). The low respiratory quotient in a *fasting patient,* and in *fever,* is due to the absence of carbohydrate in the combustion processes.

### 2. *The Apparatus of Jaquet-Grafe*

With this apparatus, the patient lies on a bed, with his head enclosed (air-tight) in a box, which is ventilated by means of an Elster gas clock; samples of the expired air are drawn off, over Hg. (Jaquet's principle), and analyzed by a very exact method (modified Palmqvist-Petterson). The temperature and barometric pressure are continuously recorded, and the amount of air passing through the box is measured. The oxygen consumption and carbon dioxid formation are, therefore, easily calculated.

### 3. *The Universal Respiration Apparatus (Benedict)*

This has been referred to above. It is especially useful for studies over brief periods, and, in all probability, it, or some similar apparatus, will be the type used in studies of total metabolism in our larger clinics.

## (c) *Rough, Approximative Methods of Studying Total Metabolism*

A rough estimate of the combustion processes of the body and energy expenditure (total metabolism) can be arrived at by carefully weighing the food ingested and keeping a record of the body weight of the patient over a considerable period.

Thus, in a diabetic woman, studied by Staehelin, the food ingested during a single day was as follows:

| | Protein | Fat | Carbohydrate | Calories |
|---|---|---|---|---|
| Herring, 98 *g* | 17.3 | 1.8 | ... | 87 |
| Mutton chop, 70 *g* | 18.9 | 2.8 | ... | 104 |
| Roast pork, 230 *g* | 80.5 | 18.9 | ... | 507 |
| Ham, 67 *g* | 16.9 | 5.4 | ... | 119 |
| Swiss cheese, 74 *g* | 17.6 | 24.1 | 3.7 | 311 |
| One egg, 45 *g* | 5.6 | 5.4 | ... | 75 |
| Butter, 54 *g* | 0.4 | 45.6 | 0.3 | 427 |
| Green peas (boiled), 80 *g* | 4.9 | 0.3 | 9.9 | 63 |
| Asparagus, 150 *g* | 3.0 | 0.4 | 1.9 | 24 |
| Total | 165.1 | 104.7 | 15.8 | 1,717 |

This diet was given for 18 days and corresponded altogether to 32,460 calories. During this period the woman excreted in the urine 343.2 g. of glucose (= 1,400 Cal.), leaving 32,460 — 1,400 = 31,060 calories for the body use, or about 1,720 calories per day. During this period, the patient's body weight remained fairly constant (varying slightly, between 100-101 kilograms). One would have expected her to have lost weight on this diet, for she did light work during the day. A normal patient, weighing 60 kilograms and working as she did, would use 2,200-2,600 calories; the patient weighing 100 kilograms might reasonably have been expected to use 30 calories per kilogram, or 3,000 calories per day. Instead of this, she kept her weight on an intake less than that required to maintain normal weight in a person weighing only 60 kilograms when at rest. Obviously, therefore, in this patient of Staehelin's, the expenditure of energy (total metabolism) was much below normal and this depended upon conditions underlying a constitutional obesity.

Such calculations are, however, but rough approximations, for, as is well known, the body weight is not an exact measurement of the state of the nutrition. The water-content of the body varies considerably from day to day, and, in pathological states (edema), might easily mislead.

For accurate studies of total metabolism, therefore, it is necessary either to use direct calorimetry, or to follow the gas metabolism (oxygen, intake and $CO_2$ output in the respired air).

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# Part XIII

Section II

## SPECIAL DIAGNOSIS OF DISORDERS OF METABOLISM

Under this caption, we shall consider:

A. States of Under-nutrition.
   1. Starvation, Marasmus.
   2. Partial Food Deficiencies (Scurvy, Beriberi, Pellagra).
   3. Cachexias.

B. States of Over-nutrition (the Obesities).

C. The Amino-acid Diatheses.

D. The Polyurias Other Than Diabetes mellitus.

E. Diabetes mellitus.

F. Gout.

The disturbances of metabolism due to diseases of the glands of internal secretion are discussed in Part XIV. The metabolic disorders accompanying infections and those accompanying diseases of the blood, the organs of digestion, the organs of respiration, the circulatory apparatus, the urogenital organs, the locomotory and skeletal systems, and the nervous system are referred to in connection with the special diseases of these several systems.

## A. States of Under-nutrition

An individual may be under-nourished, either (1) because he does not absorb enough food into his system, as in (a) prolonged hunger or starvation; (b) certain partial food deficiencies; (c) in disorders of digestion and absorption that do not permit of the assimilation of the food ingested; or (2) because (a) he destroys the food too rapidly (as in cachexias), or (b) fails to utilize the food absorbed (as in diabetes mellitus).

The disorders of digestion and absorption are discussed in Part VIII. Diabetes mellitus will be described further on in the present section. Here, under-nutrition due to starvation and under-nutrition in the cachexias will be taken up.

## 1. Under-nutrition Due to Starvation

(*Hunger Metabolism, Marasmus*)

### (*a*) *Introduction*

Careful studies have been made of people who have starved themselves absolutely for shorter or longer periods (hunger, starvation, total abstinence from food), and also of persons who have become emaciated owing to the ingestion of a faulty or insufficient diet (under-nourishment, inanition).

Studies on starvation have been made in animals and in a few men like Cetti, Breithaupt and Succi. The conditions in experimental starvation of this type are very different from those of inanition due to disease, for in the latter, aside from the insufficiency of the amount of food ingested, we have to consider the influence of the underlying disease itself upon metabolism. Moreover, in experimental starvation, the food has been suddenly withdrawn from persons previously healthy, whereas, in the cases of under-nutrition that we study clinically, the patients have usually been "running down" for a long time, during which time the metabolism doubtless undergoes certain readjustments through which its processes may be very different from those of a healthy person who decides suddenly to deprive himself of food.

### (*b*) *Total Metabolism in Starvation*

Studies of the oxygen combustion and $CO_2$ excretion in experimental starvation in man indicate a marked constancy of the amount of oxygen consumed. Quickly falling to a low level, it remains at this level without much alteration until the end of the fast. Indeed, it would seem that the oxygen consumption per kilo of body weight is not diminished, but is a little increased, for the oxygen consumption does not fall in the same proportion as does the body weight. From the tests thus far made, it would seem that a healthy man who fasts for a considerable period burns daily 27-32 calories per kilo of body weight. In persons who become slowly emaciated on account of poverty that prevents a sufficient food supply, the body as a rule shows this same extravagance in the use of the material at its disposal, the heat production rarely falling below 30 calories per kilo of body weight. There are some exceptions to this rule, which indicate that, under certain circumstances, regulatory

mechanisms can come into play, the body adapting itself, to a certain extent, to the decreased food supply by a lower flame. But these cases are exceptional, and they are in contrast with the majority of cases, which follow the rule above laid down.

The *respiratory coefficient*, however, falls to a very low level during starvation. It is usually below 0.7, the level corresponding to that when protein and fat alone are burned. Just why this occurs has been much discussed. Some assume that the protein and fat metabolized undergo decomposition along abnormal paths (Zuntz and Lehmann), a view to which some support is lent by the studies of the chemical composition of the body in starvation (Umber). Others assume that the low respiratory quotient is due merely to alterations in the ventilation of the lung, dependent upon superficial breathing; according to them, the actual metabolic changes in the body correspond to the normal burning of protein and fat alone (Jaquet).

### (c) *Protein Metabolism in Starvation*

The nitrogen excretion in the urine in *professional fasters* is not so very low; thus, in Cetti, it fell on the 8th day to 8.9 grams, or about 25 per cent less than in a fully nourished man. At later periods of a fast, very low values may be obtained, 2.82 grams nitrogen on the 21st day in Succi, and 3.4 grams nitrogen on the average between the 25th and 30th day of the fast in another faster. Other things being equal, the more fat there is in the body, the less will be the amount of protein metabolized, and *vice versa*. Similarly, the more protein present in the body at the time of the beginning of the fast, the more there will be decomposed from the beginning on.

In animals, just before death from long fasting, there is a premortal increase of the nitrogen excreted, the cause of which is not entirely clear.

In *chronic under-nutrition*, the protein metabolism behaves somewhat differently from that in experimental fasting, for the organism seems to be able to adapt itself to a certain extent to the gradually diminishing amounts of protein in the food; it can maintain nitrogen equilibrium with much smaller amounts than in normal circumstances, and a protein gain can be brought about by means of a protein intake much smaller than would be necessary in a strong healthy man.

In such states, however, there seems to be no marked tendency to economize in the number of *calories* burnt per kilo; in other words, the organism becomes relatively economical of its protein and uses fat wherever possible for combustion (P. F. Richter).

When the *partition of the nitrogen* in the urine is considered, it is found that the purin nitrogen and the ammonia nitrogen are but little altered as regards their percentage of the total nitrogen, though both are

somewhat increased. The urea nitrogen, however, may be markedly diminished in the urine in fasting. Thus, in Succi, the urea nitrogen made up only between 54 per cent and 56 per cent of the total nitrogen; normally, it makes up about 85 per cent. It is probable that the amino-acid nitrogen is increased at the expense of the urea nitrogen.

### (*d*) *Fat Metabolism in Starvation and in Under-nutrition*

When the food intake is small, or when it is entirely lacking, fat is the substance that is first drawn upon for the supply of energy. The amount burnt daily in complete fasting is remarkably constant, about the same amount being used after a week or two as during the first few days. Thus, in Succi, some 170 *g.* of fat were burnt on the 29th day of the fast, an amount equal to that on the first day, though the amount of protein consumed had been reduced to about one-third. In obese people, as much as 200 *g.* or more of fat per day may be burnt during a fast. In lean people, three or four times as much fat as protein is destroyed during fasting, and this fat yields from four to nine times as much energy as the protein burnt.

*Acetone bodies* are excreted during the fast in variable amounts, but these amounts do not run parallel with the amount of fat burnt. Apparently, the amount of glycogen available in the liver, or in the muscles, more or less determines the quantity of acetone bodies excreted. It appears that when the person is well nourished (fat) at the beginning of the fast, the excretion of acetone bodies is marked. This was the case in Succi. On the other hand, a markedly emaciated woman, practically devoid of fat, showed no acetonuria during inanition (Brugsch and Umber). The amount of *ammonia* excreted in acidosis during fasting may be very large; thus, in Succi, at one period, the ammonia nitrogen made up about 35 per cent of the total nitrogen of the urine.

### (*e*) *Carbohydrate Metabolism During Fasting and in the Under-nourished*

In animal experiments, it is found that the body maintains a certain amount of glycogen in the liver, and also in the muscles. This glycogen is probably derived from the nitrogen free residues of the amino-acid chains of the body protein that is metabolized.

It is interesting that, in such experimental animals, glycosuria may follow, if a rather small quantity of starch be fed. In other words, the carbohydrate tolerance is greatly lowered. This condition has been called *hunger-diabetes*. It is met with sometimes in man, both in professional fasters (Succi), and, occasionally, in markedly emaciated persons—the so-called *Vagantenglycosurie* of Hoppe-Seyler.

### (*f*) *Behavior of the Salts During Fasting*

Since the **chlorids** excreted normally are derived chiefly from the food, the excretion falls rapidly on fasting. Small amounts, derived from the blood and the tissues, continue to be excreted, but even these amounts grow smaller, as the body, apparently, strives hard to maintain its content in chlorin (P. F. Richter).

In the faster, Breithaupt, 3.9 *g. sodium chlorid* was excreted on the first fast day, but only 0.35 *g.* on the 6th day. According to Munk, the chlorin excreted during the fasting period is not derived from the muscular tissue metabolized, but comes from the salts of the fluids and the tissues of the body.

When food is again ingested, after a fasting period, there is marked *retention of NaCl* until the normal content is restored.

The **phosphates** on fasting are excreted in relatively large amounts. Calculations of the phosphoric acid and the total nitrogen excreted indicate that the phosphorus cannot all be derived from the protein of the muscle metabolized; a good deal of it, apparently, comes from the bones, and some of it from the nuclei of the body cells. The excretion of **calcium** is relatively high during fasting. Very little of this comes from the muscle metabolized; most of it is from the bones. The excretion of **magnesium** is also relatively increased, though the increase is by no means so great as for calcium. These substances are markedly retained when a fasting patient is again fed.

As to **sodium** and **potassium** salts, the proportions excreted during fasting are very different from those excreted normally. Under normal conditions, more of the sodium salts than of the potassium salts is excreted, owing to the composition of the food. On fasting, any sodium and potassium excreted must be derived from the tissues, in which, as is well known, potassium markedly predominates. In Cetti, the urine contained three or four times as much potassium as sodium; in Succi, on the 21st day of the fast, the proportions were as 2.3 is to 1. A similar reversal of the relative proportions is met with in fever, but in this case it is only partly due to the inanition, for in fever there is a retention of sodium salts (P. F. Richter).

If a fast be prolonged, the *total amount of alkalis* excreted steadily diminishes; when food is again given, there is marked retention, especially of sodium salts.

### (*g*) *The Body Weight During Fasting*

In death from starvation in animals, as much as 20 to 50 per cent of the body weight may be lost before death occurs.

Among human beings, professional fasters have lost during the first ten days, on an average, about 1 per cent of the body weight per day; thus, Breithaupt lost 6.03 per cent of his body weight in six days, and Cetti lost 11.16 per cent in ten days. Succi, during a 30 day fast, lost 19.04 per cent of his body weight.

Most of this decrease in weight depends upon a reduction in the weight of the fat tissue and the muscles. Next in order, the reduction in weight involves the skin, the bones, the blood, and the abdominal organs. It is a striking fact that the heart and the central nervous system are scarcely at all involved in the loss of weight.

About $\frac{2}{3}$ of the loss of weight during starvation is due to loss of water. If the faster drinks water during his fast, the loss of weight is markedly diminished and the effects of fasting can be withstood better, and for a longer time, than when no water is allowed. We do not know how long a human being can fast and survive, though professional fasters have, as everyone knows, fasted for forty days, and even longer, without succumbing. Clinically, we sometimes see patients who have lost one-third of their body weight, or even more. Animals may lose, as we have seen, one-half of the body weight before death.

The dangers of starvation are most marked in the young, least marked in the aged. It is said that a child will die in five days of hunger, even when it has not lost more than one-fourth of its body weight (P. F. Richter). Persons who are well-nourished before the fast begins, who remain quiet, and keep warm, will stand the fast better than those who are emaciated at the beginning, and than those who take exercise and expose themselves to cold.

It is interesting that, in convalescence after a long fast, or after prolonged under-nourishment from any cause, the protein gain may be very rapid if large amounts of protein are ingested; thus, in one case P. F. Richter observed a protein gain corresponding to 21 *g.* N per day, an amount larger than the total N as a whole under normal conditions.

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## 2. Disturbances of Nutrition Due to Partial Food Deficiencies

In our introduction to the study of disorders of metabolism we have referred to the growing importance of the study of *vitamins* in diet. There are certain pathological states in human beings that appear to be due to the absence of one or another of these vitamins; thus, in *scurvy*, and in *beriberi*, there can be but little doubt that a deficiency in certain substances, known at present as vitamins, are responsible, and it is pos-

sible that a deficiency in some other vitamin is the cause of *pellagra*, though, for the latter disease, the etiology has not yet been clearly established.

### (*a*) *Scurvy*

It has long been known that scurvy, or scorbutus, depends upon a food deficiency. People that do not get fresh meat and green vegetables develop characteristic symptoms of the disease (spongy swollen gums, loose teeth, edema, hemorrhagic diathesis, etc.). If a general mixed diet be resumed, the symptoms disappear. Since the laws regarding food at sea have been made rigid, there is much less scurvy than formerly. The symptoms of scurvy have been described and its diagnosis discussed in Part VII.

### (*b*) *Beriberi*

(*Kakke, Polyneuritis endemica, Hydrops asthmaticus*)

**Definition.**—Beriberi is a disease characterized by a multiple neuritis causing either atrophic paralysis, or general edema, or both, and occurring in persons whose food intake is deficient in a neuritis-preventing vitamin.

**Occurrence.**—The disease is especially common among Oriental peoples who subsist chiefly on rice, though it may occur in people whose diet does not contain rice, but is, nevertheless, deficient in vitamins. The disease is common in Japan, China, the Philippine Islands, the Dutch East Indies, and in Brazil. In 1899, as a member of a medical commission to the Philippine Islands, I had the opportunity, with Flexner, Flint and Gay, of observing a large epidemic—some 200 cases—among the Philippine prisoners at Cavité. Through the courtesy of Col. Woodhull, we were able to examine the patients carefully, and we saw many examples of both the wet and the dry types of the disease.

**Etiology.**—Until the vitamin doctrine was developed, many conflicting views regarding the etiology of beriberi prevailed.

Thus, Manson believed that under non-hygienic surroundings some germ develops, which, in its growth, gives off a volatile substance like alcohol, which causes a toxic neuritis, the germ itself not infecting the patient. Hamilton Wright believed that a bacillary infection of the duodenal mucosa resulted in toxin production, causing the neuritis. Various cocci, bacilli and protozoa have been suggested as responsible for the disease, but in no case has the proof of such an etiology been brought.

A food deficiency of some sort or another as responsible for the disease has been suggested by various clinicians. Thus, Takaki thought that an insufficient nitrogen intake is responsible, and it was found that, on increasing the protein of the ration in the Japanese Navy, the disease nearly disappeared. Deficiencies in salts (potassium carbonate), in fat, and in phosphorus, have been suggested as possible causes. For a time it was believed that the eating of fish stands in some

relation to the cause of the disease, some assuming that beriberi is due to the consumption of raw fish, others that it depends upon the ingestion of poisonous fish.

A flood of light has been thrown upon the etiology of beriberi through experimental work. Thus, in 1897, Eijkman pointed out that the disease was prevalent among the rice-eating nations whose peoples eat rice prepared in a certain way.

In the Philippines, the unhusked rice is called *palay*. On milling the rice, the husk is removed, and with it the pericarp (which contains the salts) and more or less of the subjacent aleurone layer containing protein and fat. When the latter is largely removed and practically only the starch remains, the rice is called *polished* or *highly milled rice*. Sometimes the rice is parboiled before milling; in such parboiled rice, the pericarp adheres more firmly to the grain, and, on milling, less of the antineuritis vitamin is lost (so-called *cured rice*). Under-milled rice is known as *red rice*.

It has been found that the amount of phosphorus pentoxid in rice runs more or less parallel to the amount of antineuritis vitamin present, though the phosphoric acid is not itself a component of the vitamin. Thus, rice containing less than 0.4 per cent of $P_2O_5$ will cause beriberi; whereas, rice containing more than 0.4 per cent will prevent beriberi. In some countries, laws have been passed requiring rice to contain more than 0.4 per cent of $P_2O_5$.

The experiments of Fraser and Stanconon (1909) with Javanese coolies, and the experiments of Strong and Crowell in Bilibid Prison in the Philippines, prove conclusively the relation of polished rice to beriberi and the efficacy of the administration of rice-polishings in preventing and in curing beriberi, though they found that mongo-bean or yeast is much more efficacious than rice-polishings as a curative agent.

The time required for beriberi to develop after the diet has become deficient in neuritis-preventing vitamins seems to vary somewhat. Thus, in Fraser and Stanconon's series the shortest period was 87 days, and in the majority of cases the disease does not develop until after 120-160 days. In Strong and Crowell's series, symptoms of beriberi appeared in from 61 to 75 days after the beginning of the deficient diet. Scurvy did not appear in these persons, a fact that indicates that the vitamin responsible for the prevention of scurvy is different from that concerned in the prevention of beriberi. Even before these experiments were done, Braddon had insisted upon the importance of the rice factor in the etiology of the disease.

Funk's studies on the vitamin of rice-polishings have already been described (See above). A temperature of 130° C. appears to destroy the vitamin that prevents beriberi.

In Brazil, the beriberi that occurs is not due to the eating of rice, but seems to depend upon a lack of vitamin in the other foods eaten. It is asserted that sago, boiled white potatoes, corn, grits, and macaroni, are deficient in the same

vitamin as is polished rice, and will give rise to polyneuritis gallinarum (Wellman and Bass).

It seems certain now that beriberi is not an infectious disease, and that for prophylaxis we must depend upon making sure that every person has a diet that contains enough of the beriberi-preventing vitamin. A practical illustration of this point will be found in the report of Heiser on the outbreak of beriberi in the leper colony at Culion in the Philippine Islands in 1911 and 1912. The outbreak ceased when unpolished rice was substituted for the use of polished rice in the diet.

It has been suggested by Vedder and Clark, who have made a special study of polyneuritis gallinarum, that two vitamins may be involved, one preventing neuritis, the other preventing general prostration and cardiac degeneration.

**Symptoms.**—The symptoms of beriberi are those of a *multiple neuritis*, on the one hand, and those of a *general anasarca*, on the other. According as atrophic paralysis due to neuritis or anasarca dominates the clinical picture, the cases are described as *dry* or *atrophic* beriberi, and *wet* or *dropsical* beriberi. As a matter of fact, there are many *mixed* cases, in which atrophic paralyses are associated with edema.

The disease is, as a rule, *afebrile*, though cases described in the literature as *epidemic dropsy with fever* may be examples of beriberi complicated by some infection. It may be, however, that epidemic dropsy and beriberi are two distinct diseases, though Pearse maintains their identity.

At the *onset* of beriberi, the patients complain of weakness in the legs, fatigue, palpitation and dyspnea on exertion. There is some epigastric tenderness, and as neuritis develops, hyperesthesias of the calf muscles and, sometimes, of the muscles of the hand and forearm are complained of. Slight hypoesthesias develop in the distal portions of the extremities, and localized edemas appear over the shins and malleoli, on the dorsum of the foot, over the sacral and sternal regions, and often, also, in the arms. The deep reflexes at the beginning may be slightly exaggerated. There is a moderate tachycardia, increased by any exertion, and associated with a low systolic blood pressure.

As the disease progresses, the paresis of the muscles of the arms and legs increases. The edema may either recede, or it may become very marked, resembling that of an acute nephritis, though the scrotum is, as a rule, less involved than in nephritic edema. The patients complain of a feeling of constriction in the chest. Many of those I observed in the prison at Cavité placed their hands over the sternum and evidently suffered from a distressing sensation there.

Along with the subcutaneous edema, there may be dropsy of the several serous sacs (hydrothorax, hydroperitoneum, ascites). A special feature of the multiple neuritis of beriberi is the marked involvement of the N. vagus (with respiratory, cardiac and vasomotor disturbances). When the neuritis is well developed, the deep reflexes, including the

knee-kicks, may disappear, and well-marked foot drop and wrist drop, with atrophy of the distal muscles of the extremities, develop. On electrical examination, a typical reaction of degeneration (DeR) is found. The gait is the typical "steppage gait" of multiple neuritis, wholly different from the stamping gait of tabes. The mind remains clear throughout.

In the digestive system, there may be nausea, vomiting, and epigastric distress. It is not certain whether these symptoms depend upon the involvement of the vagus in the neuritis, or upon the cardiac decompensation.

The urine varies in quantity; as edema develops, there is oliguria; on absorption of the edematous fluid, there is polyuria. Albuminuria may occur if there be marked cardiac decompensation, but there seems to be no toxic degeneration of the kidney in the disease.

The blood shows a moderate diminution of the red blood corpuscles and hemoglobin, but, otherwise, it is negative.

**Special Forms of Beriberi.**—In addition to the wet form, the dry form, and the mixed form, already referred to, several special forms have been described. These include: (1) the **rudimentary types,** which are quite common. In such cases, there may be slight weakness of the legs; hypoesthesias, and disturbances of the reflexes, or transitory edemas, dyspnea, and palpitation may be present. The diagnosis of such *formes frustes* may be exceedingly difficult. In the tropics, a diagnosis of beriberi is often made on insufficient grounds.

The most dreadful form of the disease is (2) the so-called **fulminating type,** or **acute pernicious beriberi.** In this type, the involvement of the N. vagus dominates the clinical picture. Symptoms of the acute form may develop and terminate fatally within a few hours. Such acute symptoms may develop without warning, or they may occur in the course of an ordinary beriberi, or in the course of one of the cases apparently rudimentary in type. Death may be agonizing from sudden dilatation of the right heart.

Special mention must also be made of (3) the so-called **infantile beriberi.** It is known as *taon* in the Philippines, and occurs in infants nourished by beriberic mothers (Hirota, Andrews). The children are restless, suffer from vomiting, tachycardia, edema, and cyanosis. At autopsy, there is marked dilatation of the right heart and degeneration of the peripheral nerves. If the disease be recognized, and suitable artificial food given instead of mother's milk, along with extract of rice-polishings, the infants improve rapidly.

**Diagnosis.**—When the disease occurs in large outbreaks, on shipboard, in prisons or asylums, or among rice-eating peoples, no mistake is likely to be made; but, in sporadic cases, the disease is doubtless often overlooked, or, rather, misinterpreted. Unfortunately, there is no specific

test for beriberi, but if the disease be suspected, the diet of the patient should be carefully inquired into (1) for monotony, and (2) as regards overheating (canned foods).

Beriberi must be differentiated (1) from *nephritis* (albuminuria, cylindruria, absence of signs of neuritis); (2) from *tabes* (Argyll-Robertson pupil, cerebrospinal fluid, Wassermann); (3) from *alcoholic neuritis* (anamnesis, tremor, mental symptoms); (4) from *arsenical neuritis* (edema of the eyelids, cutaneous pigmentation, arsenic in urine); (5) from the *neuritis of lead poisoning* (blue line on gums, basophilic stippling of red blood corpuscles); (6) from the *neuritis of diphtheria* (anamnesis, involvement of soft palate and of M. ciliaris); (7) from Scandinavian *ship beriberi,* according to Nocht, probably a form of scurvy (absence of neuritis; more rapid recovery on normal diet).

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## (c) *Pellagra*

(*Mal de la rosa, Mal del sole, Alpine Scurvy, Asturian Leprosy, Maidismus*)

**Definition.**—Pellagra is a disease characterized by peculiar cutaneous, digestive, nervous and mental disturbances, usually running a chronic course, with periodic exacerbations, but sometimes developing acutely and proceeding quickly to a fatal termination.

**Historical.**—The disease doubtless occurred in ancient times, but was not recognized as a definite entity until the eighteenth century, when Casal studied it in the Asturias, observing that it occurs among the peasants who live chiefly on corn and rarely eat fresh meat. The name pellagra (*pelle,* skin, and *agra,* rough) was given by Frapolli (1771).

The maize theory dates from the publication of Marzari (1810), who supported the idea that pellagra and Alpine scurvy are identical. Since 1907, manifold opportunities for the study of the disease have existed in the United States, pellagra being prevalent in an exceedingly fatal form in a number of the Southern States.

The disease is very common in Italy, in the Balkans, in Lower Egypt, in the West Indies, and in Mexico and Central America.

**Etiology.**—The cause of pellagra is not yet known, and there have been warm disputes among champions of different etiological theories. For a long time, Indian corn, or maize, was believed in some way to be responsible for the disease. Those who advocate this doctrine are known as *zeists;* those who oppose it as *antizeists.* Two of the principal champions of the zeistic theory were Marzari and Lombroso. Among the antizeists are Sambon, who assumes a protozoan etiology, with transmission of the parasite by a midge (*Simulium*), like our buffalo gnat, and Tizzoni, who believes that the disease is due to a *Strepto-bacillus.*

During the past few years a conviction has been growing that places pellagra among the diseases due to some special food deficiency, probably to a deficiency in some vitamin. The **vitamin theory** is compatible with the zeistic view, though it may hold even though the zeistic theory should turn out to be untrue.

Dyer evidently views the disease as dependent upon food deficiency, and believes that it can be prevented or cured by the use of gelatin, orange juice, or lemon juice, along with a diet of eggs, milk and well-cooked vegetables. Goldberger and other officials of the Public Health Service lay great stress upon a high protein ration in the dietary, having noticed that in an orphan asylum in which 32 per cent of the children had pellagra, the disease was much more common among the children that lived practically on a vegetarian diet that consisted largely of corn products and syrup, and in which legumes were present in only small amounts.

Some of the zeists have attributed the disease to the spoiling of corn by moulds or bacteria (*zeitoxic view*). Some assume that the disease is *anaphylactic* in nature, due to sensitization to the proteins of maize. It has even been suggested that pellagra following a maize diet results in the introduction of certain *photodynamic substances* into the circulation, and that these, under the influence of sunlight, become toxic (Rabitschek). Hirschfelder tried to find a fluorescent body in the blood serum, but was unable to do so.

Thanks to the careful studies of the Thompson-McFadden Pellagra Commission, some important facts regarding the epidemiology of pellagra are gradually being discovered; thus, in the Southern States, the disease prevails chiefly among workers in the cotton-mill *villages* rather than among those on the farms. This is in marked contrast with the observations of Sambon in Egypt, who noted a greater incidence among farm laborers in the rural districts and based his midge doctrine on the observation.

Furthermore, the Thompson-McFadden Commission found that the disease occurs five times as often among *women* (who remain in their homes) as among men (who are in their houses only at night).

The Commission could find no evidence in favor of the transmission of pellagra by ticks, lice, bedbugs, cockroaches, flies, mosquitoes, or buffalo gnats. The members of this Commission report a greater prevalence in neighborhoods where unsanitary privies are permitted, and a less prevalence where an efficient water sewerage exists.

As Stitt, referring to the work of the Commission, points out, "the peculiarities of sex and place distribution could be explained by the stable fly, *Stomoxys calcitrans*, a fly that bites viciously in the district in which they worked. This fly bites only by day and is intimately associated with human dwellings, so that the greater incidence of the disease in the women who stay at home, as against an incidence five times less in the women or men who work in the mill during the day, might be explained by the Stomoxys bites.

The Commission found it impossible to transmit pellagra to monkeys by injecting the defibrinated blood of pellagrins, though Harris asserts that he has

produced a disease like pellagra in two monkeys by injection of filtrates from emulsions made from the brain, skin and intestinal tract of patients dying of pellagra. The Commission further assert that they can find no relation pointing distinctly to corn as a cause of outbreaks of pellagra. They admit, however, that among the people affected they observed a very limited use of fresh meats.

Unsatisfactory as the present state of knowledge regarding the etiology of pellagra is, it would seem that we are on the eve of the discovery of the cause. There is good reason to believe that the disease is due either to a *food deficiency* or to some *protozoan infection.* Undoubtedly many arguments can be brought forward in favor of each. My personal

Fig. 633.—A Patient Suffering from Pellagra. The Cutaneous Lesions Are Well Shown. The Emaciation and the Somewhat Depressed State Are Obvious. (Courtesy of Dr. R. T. Dorsey, Jr., Atlanta, Ga.)

conviction is that we shall find, later on, an absence of some vitamin in the food to be responsible for the disease.

**Symptoms.**—The disease begins, as a rule, with *neurasthenic manifestations* (fatigability, insomnia, slight vertigo, feelings of apprehension), and slight *digestive disturbances.* These symptoms often appear in the winter, to be followed in the spring by more marked disturbances of digestion, including *sore mouth, pyrosis,* and *diarrhea.* The parts of the skin exposed to the sun's rays begin also to show characteristic changes in the form of a sharply delimited and strikingly symmetrical *erythema,* later becoming an outspoken *dermatitis,* desquamating over a period of

weeks or months, without healing, and undergoing marked *pigmentation* at the borders. Severe *nervous and mental symptoms* then develop (changes in the reflexes, tremor, mental depression, toxic psychoses, sometimes dementia). In the severe cases, the patients become *cachectic,* emaciating rapidly. Before the end, there may be complete *dementia,* the patients soiling themselves.

In the less severe cases, the disease tends to *recur* each spring. In some instances, a year may be skipped without an exacerbation. In the winter, the cutaneous and digestive manifestations let up, though the

Fig. 634.—The Hands in a Case of Pellagra. (After W. S. Thayer, J. H. H. Bull.)

nervous symptoms may continue. The clinical picture varies greatly according as one, or another, of the **pellagrous triad** of symptoms (cutaneous, digestive, nervous) predominate.

On **physical examination,** signs of *stomatitis* (hyperemia; red, fissured tongue, indented at the edges; salivation; spongy gums; enlargement of the regional lymph glands) are found. *Achylia gastrica* is often present, and the *diarrhea* may resemble that of dysentery. *Indicanuria* points to putrefactive disturbances within the intestine.

The *cutaneous* manifestations may be very characteristic. The main points have already been mentioned. The skin of the back of the hands and wrists takes on a dull red color, not unlike sunburn. Later, the color becomes reddish brown or slightly cyanotic, and the skin becomes scaly and atrophic. Sometimes, the skin of the hand and of the lower forearm is shed like a gauntlet. The dorsum of the foot is similarly involved, as is also that of the great toe, though the dorsal surfaces of the lateral toes often escape. The erythema may become delimited at the level of the malleoli, though in some instances it extends up the front and back of the leg like a boot. The eruption on the face involves the bridge of the nose and may spread to the cheeks and to the forehead. A *butterfly appearance,* as in lupus erythematosus, or a more general involvement—the so-called *pellagrous mask*—may be observed. A very characteristic bandlike eruption is sometimes seen at the back of the neck (*pellagrous collar*). This may extend in front to the upper part of the sternum (*Casal's necklace*), or even lower down upon the sternum like a *cravat.* The *topography* of the eruption appears to depend upon the irritating effects of the sun's rays, but any irritation may call forth an erythematous eruption in pellagrins; thus, the friction of the clothing, or an intertrigo, may elicit an erythema (peri-anal, perineal, vulvar, scrotal). Exposure to x-rays should be avoided.

Fig. 635.—Pellagra in a Child. Notice the Sharply Limited Erythema of the Hands. (Courtesy of Dr. E. J. Wood.)

The *nervous and mental symptoms* of pellagra indicate diffuse lesions within the central and peripheral nervous system, and such lesions have actually been found at autopsy by Spiller. Any of the functions (motor, sensory, reflex) may be involved, but the involvement in different cases is exceedingly irregular and not according to systems. The mentality is nearly always more or less involved, and outspoken insanity is so common that the disease is much feared on account of the danger of the

necessity of treatment within asylums. The *cerebrospinal fluid* is normal, in marked contrast with protozoan diseases involving the central nervous system.

The *blood*, aside from a moderate anemia and a relative lymphocytosis, shows no marked changes. The eosinophiles are usually below 3 per cent in the differential count. The coagulation time is normal (Hillman).

Fig. 636.—Notched Casal Collar of Erythema on the Neck of a Child Suffering from Pellagra. (Courtesy of Dr. E. J. Wood.)

In the *circulatory system*, there is arterial hypotension and evidence of lability of the vasomotor system.

In the *genito-urinary system*, no marked changes have been made out, except a tendency to vaginitis and vulvitis in the women affected.

Pellagra is ordinarily an *afebrile disease*. When fever occurs, it appears to depend upon some complication and is a *signum mali ominis*. In the so-called typhoid pellagra, the temperature may be quite high over a considerable period. The nature of this condition is not clear; it may depend upon a septicemia.

Cases of pellagra without the cutaneous manifestations (*pellagra sine pellagra*) have been described. The term *pseudopellagra*, as Stitt emphasizes, "has usually been used by those who insist upon limiting the name pellagra to those cases that fit in with their special etiological views."

**Prognosis.**—In pellagra this is exceedingly uncertain, and the physician should be cautious in giving a definite opinion. Mild cases may suddenly become very severe. The severity of the case does not run parallel with the cutaneous lesions.

Pellagra is a much more fatal disease in the United States than in Italy. With us, the mortality varies between 25 per cent and 40 per cent; in Italy, it is below 10 per cent, and recently appears to have been only about 3 per cent.

**Diagnosis.**—This is easy in the *typical cases* with cutaneous, digestive and nervous disturbances, especially when the disease is met with in a district in which it is known to prevail.

Sporadic cases, and cases in which the cutaneous manifestations are not present, or are very slight, may fail to be recognized; indeed, in many cases doubt must, or should, exist even in the mind of an expert on pellagra.

We possess no specific laboratory tests for the disease.

In the **differential diagnosis** we must separate pellagra (1) from *other forms of dermatitis* (erythema multiforme, dermatitis venenata); (2) from *other diseases of the digestive system* (other forms of stomatitis, sprue, dysentery); (3) from *other diseases of the nervous system* (ergotism, cerebral atherosclerosis, cerebral lues, the psychoses, etc.).

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## 3. The Cachexias

### (*a*) *Introduction*

**Definition.**—The term "cachexia" (*caco-*, bad; *hexis*, habit) is a clinical expression that has been used in a rather loose way to designate the bodily deterioration accompanied by subjective feelings of exhaustion met with in neoplasm (carcinoma, myoma), in Graves's disease, in severe anemias, in chronic intoxications (*e. g.*, morphinism, mercurialism, phosphorus poisoning), and in long continued fevers of infectious origin.

**Symptoms.**—Emaciation (loss of both fat and musculature); anemia; sallow tint, tendency to hemorrhagic diathesis ("cachectic purpura"), impairment of functions of digestive organs, cardiac weakness, "cachectic edema" in dependent parts, exitus.

**Pathogenesis.**—The cachexias in the narrow sense depend upon a toxic destruction of protein (Fr. v. Müller), and, in some instances, perhaps, upon catabolism of protein substances along abnormal paths, through the influence of atypical ferments (heterolytic enzymes).

These cachexias we may, with Umber, conveniently subdivide into *exogenous* cachexias and *endogenous* cachexias, according to the source of the toxic substance responsible for the abnormal protein metabolism.

Thus the source may be some parasite or some chemical substance that enters the body from the outside (*e. g.*, malarial cachexia, cachexias in septic processes and infectious fevers, cachexias following chemical intoxications with phosphorus or morphin), or it may be in the metabolism of the body itself (*e. g.*, neoplastic cachexias, thyrotoxic cachexias, cachexia of Banti's disease, etc.).

### (*b*) *Studies of Metabolism in the Cachexias*

Though the abnormal metabolic changes in the cachexias are doubtless very complex, there is evidence to indicate that it is the protein metabolism that is most perverted.

#### i. The Carcinoma-cachexia

The carcinoma-cachexia has been most carefully studied. If, in a carcinoma-cachexia, enough protein, carbohydrate and fat be given to afford a sufficient supply of calories and to maintain the nitrogenous equilibrium of the same person when in a normal state, it is found that the cachectic patient shows a nitrogen deficit. Indeed, if the toxic injury to the protoplasm be severe, even a large excess of protein may be fed without maintaining nitrogenous equilibrium. Thus, in one of F. v. Müller's patients, suffering from carcinoma, a nitrogen deficit persisted, and even increased, despite a daily intake of 21 *g.* N and 3,064 calories in the food. The increased destruction of protein in cancer may depend, in part, upon the action of atypical ferments, since many studies have shown the presence of heterolytic enzymes, capable of proteolysis, in certain carcinomata, though not in all. Not every carcinoma leads to cachexia; moreover, in cases of carcinoma-cachexia, it is probable that injurious agents, other than these atypical enzymes, are at work. Thus the red corpuscles of the blood are often rapidly destroyed (isolysins?) in carcinoma-cachexia, so that a picture closely resembling that of pernicious anemia may develop.

The increased excretion of colloidal nitrogen (Salkowski) in the form of oxyproteinic acid and other substances, and of urobilin (F. v. Müller) in the urine, while noted in carcinoma cases, is not specific for them. The ketonuria sometimes met with in cachexia appears to be due simply to the insufficient assimilation of carbohydrates (hunger-acidosis).

#### ii. The Cachexia of Grave Anemias

We regard the carcinoma-cachexia as an *endogenous* form. Similar phenomena are met with, however, in *exogenous* cachexias, like the *cachexia accompanying dibothriocephalus anemia.* Here, the toxic destruction of protein (Rosenquist) depends upon the presence of the worm in the intestine; it is independent of the degree of anemia, and it ceases as soon as the worm is expelled. The toxic substance responsible for the anemia exists in sterile aqueous extracts of the worm; it is, apparently, a lipoid substance, an oleic acid ester of cholesterin (Faust and Tallqvist), which possesses marked hemolytic properties. Whether the toxic disintegration of protein causing the cachexia is due to this same substance, or to proteolytic enzymes set free when segments of the worm are digested, has still to be found out.

### iii. The Cachexia of Hyperthyroidism

In the endogenous *cachexia of thyro-intoxication,* as seen in Graves's disease, we have to deal, at certain times only, with substances that not only accelerate the total metabolism (calories) but also cause an increased (toxic) protein degradation (F. v. Müller). Sometimes, the increased metabolism can be counterbalanced by an excessive intake in protein and in calories, especially if arsenical preparations be used at the same time to slow metabolism. Sometimes, a strumectomy will stop the increased catabolism. I have often observed a rapid increase in weight after strumectomy. In one case, observed accurately by Matthes, a nitrogen deficit existing before operation gave way soon afterward to a nitrogenous equilibrium easily maintained.

### iv. The Cachexia of Banti's Disease

Another endogenous type is the *cachexia of Banti's disease.* If this cachexia be studied at its beginning, before ascites develops (since this disturbs metabolic studies through retention of nitrogen in the ascitic fluid), a toxic disintegration of protein is demonstrable. As is now well known, Banti's disease can be cured if splenectomy be performed early. It is interesting to note that in two splenectomized cases studied, the toxic catabolism of protein ceased promptly after the operation (removal of the poison forming spleen).

In the light of these newer studies, the cachexias, formerly so ominous, now look less formidable. With means of diagnosis permitting of earlier recognition of a toxic catabolism of proteins, we may often, as Umber emphasizes, be fortunate enough to remove the source of the toxic substance—a beginning carcinoma, a part of the thyroid gland, a tapeworm, or a diseased spleen.

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# B. States of Over-nutrition

## 1. Introduction

When an excess of nourishment is taken and the digestive and assimilative powers are good, a human being like an animal will grow fat or obese. "Obesity" is a term applied to several different conditions, which have, in common, an excessive development of the fatty tissues of the body. We shall in this section, therefore, consider "The Obesities," for it is desirable to emphasize the fact that "obesity" does not represent a single disease entity.

### (*a*) *The Fatty Tissues and the Fat Metabolism in Healthy Persons That Eat and Exercise Normally*

The amount of fat in the body of an adult person, who is neither obviously thin nor fat, may vary within tolerably wide limits (10 to 20 per cent. of the body weight), women being normally a little fatter than men. The fatty tissues include (1) the subcutaneous tissues (2) the omental and mesenteric tissues of the abdomen, and (3) the interstitial tissues, chiefly of the muscles, and, to a less extent, of the viscera. Certain of the cells of parenchymatous organs, especially the liver cells, act as temporary storehouses of fat; the liver cells thus perform for fatty substances a function similar to that subserved for carbohydrates and for purins.

Human fat is fluid at the body temperature; about three quarters of it, as we have already seen (See Metabolism of Fats), is triolein, the rest tristearin and tripalmitin, the mixture having a melting point of about 20° C. The food fat can apparently be directly deposited as such in the fatty tissues, the fat of these deposits varying in constitution with the nature of the food fat; the fat in the liver cells appears, on the other hand, to be constant in composition, independent of the source of the fats of the food. In diabetes and in phosphorus poisoning, however, fat can be transferred from the fatty tissues to the liver cells and to the heart muscle cells, in which event foreign fats (*e. g.*, mutton fat) can sometimes be demonstrated in these cells.

The fat of the fatty tissues, besides being derived directly from the fats of the food, can originate in (1) carbohydrates of the food, when eaten in excess, (2) probably, also, in small amount from the deaminized amino acids of proteins and (3) possibly, in small amount, from alcohol. The amount of water drunk appears to exert but little, if any influence upon the amount of fat produced, or burned, in the body (contrary to popular belief).

Normal adults, unless they change their habits of life markedly, vary but little in weight. Even when they pay but little attention to variations in the food set before them, they unconsciously adapt their food intake to their food need in such a way that the body weight remains fairly constant and within normal limits. But should a normal person radically change his habits of life, either in the way of increasing his food intake or of decreasing the amount of muscular exercise, as often happens after marriage, after middle life, or after "material success" in life, he may gradually, or quickly, become obese **(exogenous obesity).** In certain patho-

logical states (see below) in which the fires in the body burn lower than normal (the "total metabolism" being too low), amounts of food and exercise that would not lead to increase in weight in a normal person of the same size will be followed by obesity **(endogenous** or **constitutional obesity).**

It is obviously, therefore, of great clinical importance to know the normal caloric need of persons of different size, and, in cases of obesity, to determine whether the storing of fat is exogenous or endogenous in type; sometimes we find both exogenous and endogenous factors responsible in one and the same person.

### (*b*) *Determination of the Normal or Ideal Body Weight*

Various formulae have been set up for *ascertaining the normal weight of persons of different size.* The formulae of v. Noorden, of Bernhardt, of Broca, of Oeder, and of Guthrie may be mentioned.

**Von Noorden's Formula:** Normal body weight = height in cm. × 430 to 480 g.

Thus, if the height be 170 cm., the normal weight varies between 73.1 and 81.6 kg.

**Bernhardt's Formula:** Normal weight $= \frac{(L \times C)}{240}$ kg., when L is the height and C the chest circumference in cm.

Thus, if L be 170 cm. and C be 95 cm., the body weight will be $\frac{170 \times 95}{240} = 67$ kg. If we divide by 200 instead of by 240 we obtain a value in kg. that represents the maximal weight within the limits of normal; if it be exceeded, the patient must (in the absence of edema, etc.) be regarded as obese.

**Broca's Formula:** Normal weight = (height in cm. — 100) kg.

Thus, if the height be 170 cm., the normal weight is 70 kg.

**Oeder's Formula:** Here a value known as the proportional height, or length (pL), is used, by which is meant twice the distance (in cm.) from the vertex to the middle of the symphysis pubis:

For men: Normal weight = (pL — 100) kg.

For women: Normal weight $= \frac{(pL - 100 \quad \frac{pL \times C}{200})}{2}$ kg.

in which C = the mean chest measurement.

**Guthrie's Formula:** In calculating the ideal weight of patients in my private service, Dr. Clyde G. Guthrie has made use of the following formula: Ideal weight = 110 lbs. + (5.5 × number of inches taller than 5 feet).

Thus if the height be 5 ft. 10 inches, the ideal weight is 110 + 5.5 × 10 = 165 lb.

### (c) *Determination of the Normal Food Requirement (in Calories)*

Having determined what the ideal weight for a given person is, the next important thing is to ascertain the normal food need (in calories) for that person. For practical clinical purposes, this will be found by the formula:

Average food need (in calories) for adults doing light work

$$= \text{Ideal weight in kg.} \times 35.$$

$$= \text{Ideal weight in lbs.} \times \frac{35}{2.2}$$

Even the normal persons taking ordinary exercise vary, however, somewhat in their food needs; the caloric need in individuals doing hard labor will amount to about 45 calories per kg. of calculated ideal weight.

The above practical formula has been worked out on the basis of more exact physiological studies of total metabolism. As a matter of fact, the total metabolism goes parallel not to the body weight but rather to the total surface of the body (Rubner). The area of the body surface can be calculated approximately from the body weight by an application of v. Meeh's formula, which is based on the observation that, for bodies of similar shape, a definite relation exists between surface and contents:

Surface in square meters $= k \times \sqrt[\frac{3}{2}]{\text{weight of the body in } kg.}$. The constant ($k$) has been found for man to be 12.3. The formula does not, however, yield wholly accurate results. For children, J. Howland gives a formula that is more accurate.

The daily caloric need per square meter of surface varies between 1,000 and 1,300 calories, that is, between 42 and 54 calories per hour for the majority of persons (Rubner). In fasting persons at rest, the combustions amount to 700 or 800 calories for 24 hours for each square meter of surface (Magnus-Levy), *i. e.,* to 29 or 34 calories per hour. Lusk's figures vary between 31.7 and 37.7 calories per hour. On muscular exercise, for every calory used in work, 2 or 2½ calories will be used and given off as excessive heat, and the total metabolism correspondingly increased over the value for a person at rest.

### (d) *The Pathogenesis of the Obesities*

We distinguish (see above) between (1) *exogenous obesities,* in which the persons affected have normal combustive powers, and (2) *endogenous obesities,* in which those affected have lower combustive powers than normal.

**When the combustive powers are normal,** if the food intake (in calories) exceed the need of energy (in calories), for work and heat, fat will begin to accumulate. This is why exogenous obesity is sometimes spoken of as the "obesity of overeating and of laziness." Thus, if the food intake exceed the food need by as little as 200 calories a day (represented by say 70 g. of white bread, 25 g. of butter or 30 g. alcohol),

combustible material corresponding to some 73,000 calories (= 8 kg. fat or 10 kg. adipose tissue) could be stored up in the course of a single year, provided there were no heightening of the combustive processes in the body. Fortunately, in healthy persons, appetite on the one hand, and muscular exercise and heat production on the other, are reciprocally so related that the food intake corresponds very closely to the food need. But changes in position in life (marriage, material success), and in time of life (middle age), often markedly alter the habits of eating and of exercise, in which event the unconscious self-regulating mechanism may prove insufficient; the balance between caloric intake and caloric need becomes disturbed, so that the patient emaciates, or grows fat, according to the direction taken by the disturbed balance. An excessive appetite (Umber's "dysorexia") may result from bad example; one of two married people may lead the other to eat excessively, or children may early indulge too freely in food, owing to the constant example set by gluttonous parents. According to Sohlern, there is a constitutional tendency to abnormally large appetite in people born with large abdomens, while people born with small abdomens tend to be relatively small eaters, owing to the fact that, through quick rise of the intragastric pressure, the appetite is prematurely satisfied! Since, in exogenous obesity, the metabolic processes go on at a normal rate, the obesity is removable by getting rid of the external causes, *i. e.,* by decreasing the caloric intake and by increasing the amount of muscular exercise, though it must be kept in mind, as Friedrich Müller emphasizes, that "Fat is capital and bears interest, viz.:—lessened muscular activity, and lessened heat dissipation."

**When the combustive powers of the body are subnormal,** a caloric intake that would, in a normal person of the same size, exactly balance the caloric need, is found to be excessive, and so fat easily accumulates despite "moderate eating." It has been definitely proven by v. Bergmann, that in certain obesities, the total metabolism (calories) goes on at a lower level than normal. This observer placed obese persons in a Voit-Pettenkofer respiration-apparatus, and found that, in certain of them (at rest), the daily values in heat production per square meter of body surface fell far below the normal. In such cases, we have, he believes, to deal with a true metabolic anomaly—a so-called "constitutional" or "endogenous" obesity. But very low values for the total basal metabolism have been found also in non-obese persons; thus a minimal metabolism of 618 calories per square meter of body surface was found in a non-obese person by Löwy and Hirschfeld, whereas the lowest value got by v. Bergmann in obesity was 662 calories; and in certain non-obese, stuporous insane patients Grafe got values as low as 491.4 calories, comparable with the values obtainable in myxedema. More important than these studies limited to the basal metabolism for a

short period, would seem to be the studies of the total energy balance extending over at least twenty-four hours. Three careful experiments by v. Bergmann prove that, in obesity, the total metabolism may be abnormally low. And clinical tests, in which the food intake is exactly controlled, the N-balance studied, and a body weight chart kept (von Noorden, Umber) support this view. Recently, there has been a revival of the doctrine that the rate of metabolism may vary with variations in the food intake—the body working "economically" when the intake is small, "extravagantly" when the intake is abundant (so-called *Luxus-consumption*). It is possible that a failure to readjust the rate of metabolism to larger intake may be a factor in the origin of some cases of endogenous obesity (Grafe and Koch).

The exact mechanisms underlying the several forms of endogenous obesity have still to be studied. In certain of the "constitutional obesities," abnormalities in the glands of internal secretion seem to be responsible; thus the obesity of dystrophia adiposogenitalis is probably due to *hypo-hypophysismus;* that of beginning myxedema to *hypothyroidism,* hence the term "thyrogenic obesity"; that of eunuchoidismus, that following castration, and that following the menopause, to *hypogenitalism* (*q. v.*). In these obesities due to disturbances of internal secretion, the oxidation processes of the body appear to be less active than normal, and the body weight is not easily reduced even by a "meager" diet, unless the oxidative processes be made more active, either by supplying, artificially, the substances of the internal secretion that are defective, or in some other way.

In Dercum's disease (*adiposis dolorosa*), and in certain forms of *localized lipomatosis* (*q. v.*), the pathogenesis is as yet far from clear; besides disorders of endocrine glands, we have, in them, to consider also the possibility of trophic influences exerted through the nervous system.

Recent writers (v. Bergmann, Rosenfeld, Gierke) incline to the view that in general obesity and in localized lipomatosis, a highly active rôle must be ascribed to the cells of the adipose tissues themselves; they think that in people with "lipomatous tendency," the fat is built up from carbohydrates in the cells of the adipose tissue, in other words, that the latter is not simply a "warehouse" for fat but is also a "fat factory." Still other workers emphasize the necessity of considering, in obesity, not simply the "energy balance" but also the actual "material side" of metabolism. The earlier views of the "specific dynamic action" of the foodstuffs (Rubner) are undergoing revision. In the United States, especially, the studies of Folin, Lusk, and Benedict favor the opinion that we must distinguish between the processes of anabolic or storehouse metabolism, and catabolic or disassimilatory metabolism. Lusk urges that we consider separately (1) a "basal metabolism," regulated by the organs of the body, even when no food enters the blood from the digestive tract, (2) a "plethora metabolism" due to carbohydrate or fat metabolism in the blood absorbed from the digestive tract, and (3) a metabolism due to the stimulus of amino acids." These new principles have not yet been applied to the clinical study of the obesities.

According to Wacker and Hueck (1913), an increase of the cholesterin-content of the food tends to increase the body weight and the warehousing of fat.

### (e) *Symptoms Manifested by the Obese*

The obese, especially if they have good muscles, may not complain of symptoms until a long time after the fat has begun to accumulate. I have often been struck by the agility sometimes exhibited by obese persons; it is not uncommon to see a woman who weighs 200 pounds dancing more easily, and with obviously greater pleasure, than her slenderer associates! But sooner or later, especially after middle life, the fat is felt as a burden. Some one—I think it was Ebstein—has divided obesity into three stages: the *enviable* or *majestic* stage, the *comical* stage, and the *pitiable* stage. In the first stage we deal with the "comfortable fat" of the moderately overnourished person; in the second, with the clumsiness and unwieldiness that excites a smile, and, in the third, with those monstrous caricatures of humanity represented by the extreme cases of obesity, in which the heart begins to fail, and cyanosis, dyspnea and edema appear.

Fig. 637.—Obesity. A Man, 23 Years Old; Weight, 334 Pounds. (Med. Service J. H. H.)

Slight dyspnea, palpitation, excessive perspiration, and fatigue on exertion, especially on climbing stairs or on walking uphill, may be the first symptoms to be noticed. The excessive weight of the body gives the muscles and the heart more work to do than normal. Respiration and circulation are impeded by the abdominal fat. The fat tends to mass itself on the trunk and in the proximal parts of the extremities. On the abdominal wall it may hang down like an apron, covering the genitals. Edema of the legs and varicose veins may result from the increased intra-abdominal pressure; this edema must be carefully distinguished from that due to myocardial insufficiency so common in the later stages of obesity. Flat foot and villous arthropathy of knees and ankles are common (due to the weight). Atherosclerosis and arterial hypertension often complicate

the picture of obesity, especially in the alcoholic. The myocardial insufficiency, so common in the obese, seems most often to be due to a weakening of the heart muscle through infiltration of the heart wall with fatty tissue —the "steatosis cordis" of Sternberg. Sudden heart failure and death after a hearty meal in hot weather, during sea bathing, or during a cold bath in typhoid, is not uncommon. The obese are especially prone to hernia, to constipation and to hemorrhoids. They sweat easily, as a rule, and often suffer from intertrigo, furunculosis, and moist eczema. Sciatica and other neuralgias are common. In fat women menstrual disturbances are common. In fat men impotence is not rare, as might be expected, especially in hypophyseal cases.

The frequency of diabetes and gout in families with a tendency to obesity has often been commented upon. The obese are often patients of plethoric habitus; emphysema and chronic bronchitis frequently co-exist.

The obese do not resist infections well; the mortality is high in typhoid and in lobar pneumonia among the obese. Surgeons dislike to operate on very obese patients.

Physicians are sometimes responsible for the development of obesity through ill-directed rest and feeding cures, especially in the nephropathies, in tuberculosis, and in the neuroses. In patients suffering from renal disease, the restriction of nitrogenous food and the ordering of a diet rich in carbohydrates may lead to obesity unless the caloric intake be carefully watched. In tuberculosis sanitaria the excessive food intake formerly urged is now as a rule avoided. The largest contingent of the therapeutogenous obese has its origin in the rest cure treatments of the psychoneurotic; the profession is awakening to the danger, however, and is seeing to it that, in overcoming states of under-nutrition, care shall be taken to avoid obesity by changing the "rest cure" into an "exertion cure" after the normal weight has been reached.

### (*f*) *Diagnosis of the Obesities*

When a patient is undressed, a glance at the body will usually tell us whether he is over fat or not. But a comparison of his actual body weight with his "ideal weight," calculated according to one of the formulae given above, permits of a more exact judgment. One would scarcely regard the surplus as serious unless, in an adult, the ideal weight is exceeded by from 30 to 50 pounds (15-20 kg.). Any excess of weight above the normal, however, even an excess of 8 or 10 pounds, should be regarded as a signal to alter the mode of life.

If obesity exist, the diagnosis should include a determination of its character (exogenous or endogenous). If the weight does not decrease gradually when the patient is placed upon a reducing diet (17 to 20 calories per kilogram of his calculated ideal weight), or if, after a begin-

ning reduction on such a dietary, the metabolism soon adjust itself to the meager intake so that the reduction does not continue, it is safe to conclude that the case is one of constitutional (endogenous) obesity, which will require the administration of organ extracts (thyroid, hypophysis) to accelerate the combustion processes. In large clinics the combustive powers may, through determination of the "energy balance," be actually tested in confirmation by direct or indirect calorimetry, but the methods are not suitable for use in general practice, and they are, moreover, if the procedure outlined above be followed, practically dispensable.

Fig. 638.—Adiposis dolorosa, or Dercum's Syndrome; Generalized Diffuse and Nodular (Mixed) Form. (After I. P. Lyon, Arch. Int. Med.)

If the obesity prove to be exogenous in type, the diagnosis should not stop short of determining the extent to which food intake and lack of exercise, respectively, are responsible, in order that the therapy may be rationally undertaken. In exogenous obesity the patient may have an excessive appetite; he may have too small a number of meals, and so eat excessively at each; his diet may not contain enough calorie-poor filling foods; he may eat too rapidly, not masticating or insalivating the food properly; or he may have fallen into habits of laziness, taking too little physical exercise, and becoming mentally torpid and phlegmatic, so that he ceases to make the many muscular contractions that characterize the alert and sanguine individual and do much toward keeping the latter thin.

If the obesity be of the endogenous type, the diagnosis should extend to an analysis of the states of the endocrine glands, based upon investigation of the size and functions of the hypophysis (visual fields, carbohydrate tolerance, x-ray of sella turcica), of the thyroid (colloid struma,

myxedema, cretinism, x-ray, etc.), and of the genital organs. It is to be remembered that the administration of thyroid extract may, by virtue of its power of increasing oxidation, cause reduction in weight in both exogenous and endogenous obesity; its effects are not limited to the thyrogenic endogenous cases.

Even when obesity exists, the diagnostician must consider carefully whether it is wise to undertake a reduction cure or not, and if he decide in the affirmative, should weigh all the circumstances before concluding as to the extent and the rapidity of reduction that is advisable. Reduction cures are to be undertaken most cautiously, if at all, in young children (as they easily become anemic), and in the old (as they easily grow cachectic). Society women, who desire a reduction of weight from reasons of vanity, should not be abruptly turned away, even though the weight is not strikingly excessive; to keep them out of the hands of quacks, to whom they would otherwise resort, the family physician will do well to undertake the hygienic direction of the patient, correct any faults of diet or of exercise that may exist, and gradually educate her regarding the importance of the maintenance of a normal condition of nutrition and the best way to arrive at it.

Fig. 639.—Typical "Fat-neck" or Symmetrical Diffuse Lipomatosis of Neck. (After I. P. Lyon, Arch. Int. Med.)

In planning reduction cures it is not necessary, nor often desirable, to follow any of the systems (Banting, Oertel, etc.) formerly so popular; for what is important is (1) to lessen the caloric intake, while at the same time maintaining a suitable partition of the protein, carbohydrate, and fat in the food, (2) to increase the muscular exercise, and (3) in case of need to accelerate the rate of metabolism. After providing sufficient protein (say 100 g.), we arrange a dietary, in which the intake in calories, instead of corresponding to the normal maintenance requirement (30-35 calories per kg. of calculated ideal weight), is reduced to a much lower amount say, four-fifths, three-fifths, or, in rapid reduction cures, two-fifths, of the normal maintenance requirement; that is, to 28, 21, or 14 calories per kilo of calculated ideal weight. The idea is, of course, to give a diet that

does not supply as much energy as the body spends, so that, to make up the deficit, the body will withdraw fat from its warehouse and burn it. But care must be taken to draw only upon the body fat, not upon the body protein; we must, in every reduction cure, avoid a negative nitrogen balance.

With the aid of Atwater and Bryant's lists (see Locke's Food Values), or with those set up by Schwenckenbecher, it will be easy for the general practitioner to plan dietaries, variable within rather wide limits, which are entirely suitable for the purpose. Tables that deal with the unprepared foods are of very little practical value here; and we must be grateful that we are now provided with tables that deal with the various foods "ready to serve."

In a table already given, examples are cited of various foods with their caloric values (per 100 g.), and their content in protein, carbohydrate and fat.

A convenient method of arranging the diet in obesity has been suggested by Umber, who advises a "skeleton diet" of about 880 calories, containing 93.7 g. protein; this is then supplemented, according to the needs of the particular patient, by an "accessory diet," consisting of given portions of foods, each "accessory portion" corresponding to a food value of 100 calories. His scheme is as follows:

*Skeleton Diet (= 880 Calories):*

*Morning:*—200 c.c. coffee or tea, with 20 c.c. milk; 50 g. Simon's bread, or 30 g. white bread.

*Forenoon:*—100 g. fruit.

*Noon:*—200 g. roast meat, 200 g. green vegetables boiled in salt water, 80 g. fruit.

*Afternoon:*—150 c.c. coffee, with 20 c.c. milk.

*Evening:*—100 g. meat, 100 g. green vegetables, 20 g. Simon's bread, 200 c.c. tea.

*At bedtime:*—100 g. fruit.

*Accessory Diet (Each Portion = 100 Calories):*

80 g. roast beef; 200 g. oysters; 40 g. white bread, graham bread or rye bread; 20 g. Zwieback; 12½ g. butter; 20 g. Swiss cheese; 25 g. sugar; 100 g. potatoes; 30 g. rice, peas, beans, or buckwheat; 20 g. flour; 200 g. apples; 150 g. apple sauce; 500 g. cranberries; 150 g. milk; 150 g. wine; 30 g. brandy or whisky.

*Accessory Diet of Filling Foods of Low Caloric Value:*

| | | | | | |
|---|---|---|---|---|---|
| 100 g. | cooked | asparagus | = | 43 | calories. |
| " | " | green beans | = | 20 | " |
| " | " | green peas | = | 108 | " |
| " | " | tomatoes | = | 20 | " |
| " | " | spinach | = | 52 | " |
| " | " | turnips | = | 40 | " |

If *myocardial insufficiency* have already complicated the obesity before the patient consults the physician, the cardiac state should first receive attention (rest, Karell diet, strophanthin, theocin). When the edema has disappeared and the heart is again compensated, a more exact analysis of the conditions underlying the obesity may be undertaken.

*Rapid reduction cures* are best undertaken only in clinics or sanitaria; if a patient remain at home, the slower methods (diet, graded exercises, Bergonié's faradism, hydrotherapy, etc.) are safer. The dangers of placing thyroid tablets in the hands of patients not under strict control and observation cannot be too strongly emphasized. Most clinicians of experience are familiar with the lamentable sequence in certain cases.

An interesting attempt to stimulate oxidation locally in order to remove local fat deposits on the abdomen has been made by Kaufmann, who injects "leptynol," a colloidal solution of palladium in lanolin, directly into the subcutaneous fat. Injections of 80-100 mmg. are made at intervals of a fortnight. I have had no personal experience with this preparation, though some authors (*e. g.*, Gorn) report good results. The remedy is said to fail entirely in Dercum's disease. My surgical colleagues often remove large masses of fat from the abdomen by excision ("lipectomy").

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# C. The Amino-acid Diatheses

## 1. Definition

As we have seen in our introduction to the study of metabolism, proteins are long chains of amino-acids, which, in the body, are split up into the constituent acids. These amino-acids are used, in part, in the synthesis of body proteins, but, in larger part, they undergo catabolic change —deaminization and oxidation—to be excreted as urea, $CO_2$ and $H_2O$. The sulphur of the S-containing amino-acids is excreted in the urine as sulphates or as neutral sulphur.

Now, just as at one stage of carbohydrate metabolism the body may, in diabetes, lose the power of further catabolizing d-glucose, so in protein metabolism the body may in disease lose the power of further catabolizing, at a certain stage, one or more of the amino-acids to normal end-products. Such a disturbance of intermediary metabolism is known as an *amino-acid diathesis.*

Of these amino-acid diatheses, three great groups of cases have already been the object of serious study: (1) a group in which a derivative (*homogentisic acid*) of the aromatic amino-acids, *tyrosin* and *phenylalanin,* is predominantly involved, and in which alkaptonuria and ochronosis are the principal clinical phenomena; and (2) a group in which *cystin,* a cleavage product of arginin, is predominantly involved, and in which cystinuria is the principal clinical phenomenon; and (3) a group in which *lysin* and *arginin* are predominantly involved, and in which the principal clinical phenomenon is the appearance of certain *diamins* (cadaverin and putrescin) in the urine—the so-called "diaminuria."

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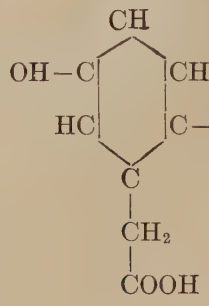
## 2. The Homogentisic-acid Diathesis

### (a) *Nature of the Diathesis and of Alkaptonuria*

This is clinically the most important amino-acid diathesis that has thus far been studied. Our knowledge of it dates back to the discovery (1859) of **alkaptonuria** (Boedeker), *i. e.,* of a urine that, of normal color when passed, turns dark brown on the addition of alkali and the absorption of oxygen. The name *alkaptonuria* (Gr. *kaptein*) refers to the strong avidity for alkali. It has been shown that the substance in the

urine responsible for the condition is *homogentisic acid.* This substance is, chemically, a benzol ring, in which H-atoms in the 2d and 5th position are replaced by OH and in the 4th position by a side chain of 2 carbon atoms (acetic acid), thus:




2-5-Dioxyphenylacetic acid, or Homogentisic acid

### (*b*) *Sources of the Homogentisic Acid*

Two of the amino-acids of protein, viz.: (1) *tyrosin* and (2) *phenylalanin,* are the mother substances of this homogentisic acid. Baumann thought that the acid arises through a pathological fermentation in the intestine, but the view first advanced by A. E. Garrod that this acid is a normal intermediary product in protein catabolism is now generally accepted. Since, in protein digestion, tyrosin is split off before phenylalanin, the earlier homogentisic acid, after a single protein feeding, comes from tyrosin, the later from phenylalanin. The amount of homogentisic acid excreted in patients suffering from this diathesis, depends chiefly upon the content of the protein of the food in tyrosin and in phenylalanin; thus casein and fibrin are richer than other proteins in these amino-acids. The alkaptonuric patient can use tyrosin and phenylalanin for the synthesis of his own body proteins (Abderhalden), but in the catabolism of the body-proteins as well as of the food-proteins, the process is held up at the homogentisic-acid stage, so that the homogentisic acid of the urine is partly "endogenous" and partly "exogenous" in origin. This metabolic anomaly appears to be referable to an insufficiency of activity of a certain ferment (*tyrosinase*) in the body tissues.

Even the normal body cannot catabolize more than a certain amount of homogentisic acid. Thus, if 50 *g.* l-tyrosin be swallowed by a healthy person, homogentisic acid appears in the urine (Abderhalden); it would seem probable, therefore, that the normal "homogentisic-acid tolerance" is less than that equivalent to 50 *g.* l-tyrosin. The path followed by tyrosin and phenylalanin (so-called homogentisic-acid formers) on their way to homogentisic acid is rather complex and need not be entered into here.

It is interesting that *tryptophan* (a third aromatic amino-acid constituent of protein) is not a homogentisic-acid former, but is normally catabolized by the alkaptonuric (Neubauer).

### (*c*) *Symptoms of the Homogentisic-acid Diathesis*

The *urine* (alkalinized) turns brown on standing and yields the reactions for homogentisic acid (See Part IX). The patient's linen may be

stained with black or brown spots, not removable by soap and water. As much as 7-16-25 g. of the acid may be excreted daily.

The acid may be present in the blood serum, in the sebum and in the cerumen, but it is absent from the sweat and from the feces.

Alkaptonuria may occur as a *family* disease, usually in one generation, though sometimes in more than one. *Males* are more often affected than females.

The **alkaptonuria** may sometimes be *intermittent,* but absence of spontaneous darkening of the urine does not exclude the diathesis!

In later life, **ochronosis** or "bluing of the cartilages of the body" often develops in alkaptonurics. The homogentisic acid (or a derivative of it) appears to be *cartilagotropic.* The first instance of ochronosis to be described was observed by Virchow (1865) at an autopsy; the cartilages of the thorax, larynx and bronchi, nose and ears, as well as the intima of the arteries, were stained an "inky black." The relation of this ochronosis to alkaptonuria was fully established by Osler and others. The ochronosis is often recognizable *intra vitam* by the dark blue discoloration of the ear cartilages and of the alae nasi showing through the skin; by a brownish discoloration of the sclerae of the eyes lateral from the cornea; by a greenish-brown staining of the sebum in the axillae; and by a brownish-black cerumen.

In ochronotic patients, severe *arthropathic symptoms* may develop. The clinical symptoms, x-ray findings, and post-mortem conditions correspond to those of "hypertrophic osteo-arthritis" (Allard and Gross; Umber), and we are doubtless justified in using the term **"osteo-arthritis alkaptonurica"** to designate such cases.

### (*d*) *Methods of Influencing the Amount of Homogentisic Acid Formed*

Since, in long-standing alkaptonuria, ochronosis and osteo-arthritis are prone to develop, means of diminishing the production of homogentisic acid have been sought. No way of decreasing the endogenous component has, as yet, been devised, but the exogenous component may be reduced in amount by dietetic restriction (Chittenden's protein minimum, which amounts to 0.7-0.88 protein per kg. of body weight; selection, in the dietary, of proteins of low content in tyrosin and phenylalanin).

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# 3. The Cystin Diatheses

## (*a*) *The Chemistry of the Cystins*

Cystin occurs, preformed, in the *arginin* of many proteins. There are *two* isomeric cystins:

(1) $CH_2$. SH — CH. $NH_2$ — CO. OH = *alpha-amino- eta-thio-glycerinic acid.*
(2) $CH_2$. $NH_2$ — CH. SH — CO. OH = *alpha-thio- eta-amino-glycerinic acid.*

The disulphid of the former crystallizes in the form of hexagonal plates; this was obtained early as the *cystein* of horny substances and was called *protein cystin;* it yields the pure amino-acid on oxidation, and it also forms hexagonal crystals.

The second cystin crystallizes in needles; it is the cystin found in certain urinary calculi, and has been called *stone cystin.* Normal human beings catabolize these two cystins, both of exogenous and endogenous origin, about $\frac{2}{3}$ of the sulphur being excreted in the urine as sulphates, $\frac{1}{3}$ as neutral sulphur. Normal urine does not contain even a trace of cystin.

## (*b*) *Cystin Stones*

In 1810 Wollaston discovered cystin in a urinary calculus. Cystin stones are so rare that they have been designated "urinary jewels." They are usually small, round stones, of a dirty yellow tint. They may arise either in the pelvis of the kidney or in the bladder. They show well in x-ray plates. Though at first thought to consist always of "stone cystin," some of them have been found to consist wholly of "protein cystin" (See above); indeed both varieties of cystin have been found in a single stone, both hexagon crystals and needles being visible on microscopic examination of thin sections. Secondary lamellae of other urinary salts may be deposited upon primary cystin stones.

### (*c*) *Infiltrations of the Organs with Cystin*

These are met with occasionally in the liver and in the kidneys (Abderhalden). When cystin cannot be catabolized, the tissue fluids easily become over-saturated, leading to formation of deposits in the parenchymatous organs. One is reminded of the tophaceous deposits of urates in gout, though urates seem to be more "arthrotropic," cystin more "organotropic."

### (*d*) *Cystinuria*

**Occurrence.**—In cystinuria (aside from the temporary forms met with in phosphorus poisoning and in acute yellow atrophy of the liver) we have to deal with the chronic excretion of cystins in the urine, owing to the inability of the body to catabolize these amino-acids to sulphates and neutral sulphur. In mild cases all amino-acids except one, or other, or both, of the cystins can be normally catabolized, but hexagons of cystin (1), or, less often, needles of cystin (2) appear in the urinary sediment either spontaneously or after the addition of acetic acid and concentration (See Part IX). In most cases of cystinuria, the metabolic disturbance is more severe, and involves not only the catabolism of the thio-amino-acids (cystins), but also, to a certain degree, that of other amino-acids. Thus spontaneous *diaminuria* (*q. v.*), in which derivatives of the diamino-acids, *lysin* and *arginin,* appear in the urine, may be associated with cystinuria. A spontaneous *monaminuria* has also been observed in cystinurics (*tryptophan,* by Garrod and Huntley; *leucin* and *lysin* by Abderhalden and Schittenhelm). Again in the absence of the spontaneous appearance of other amino-acids or their derivatives in the urine, they may be made to appear in some cystinurics by giving the pure acids by mouth; thus in certain cystinurics if 6 g. of tyrosin be taken, 5 g. will be excreted as such in the urine, and if 5 g. of aspartic acid be swallowed, 3 or 4 g. will appear in the urine unchanged (*alimentary monaminuria*). A similar *alimentary diaminuria* can sometimes be demonstrated by feeding lysin or arginin. Such tests are valuable in determining the lowered "tolerance" for the various amino-acids in the cystin diathesis.

That a monaminuria or a diaminuria appears in such cases only when the pure acids are given by the mouth supports the view of Umber that there is an essential difference between the catabolism of the amino-acids when presented "ready made" to the body and the catabolism of these acids as they appear *in statu nascendi* in the normal digestion of protein foods.

In the mildest cases of cystinuria, it may be only the *endogenous cystin* that cannot be catabolized, for a number of observers have shown that, in such instances, the cystinuria may be entirely independent of the protein or of the amino-acid intake (*exogenous cystin*). Thus, sometimes,

cystin itself, given by mouth will be normally catabolized, despite the continuance of an endogenous cystinuria, and even cystin injected subcutaneously may be partially oxidized; in such cases, various pure amino-acids (tyrosin, aspartic acid, glycocoll) given by mouth may be normally catabolized. To the establishment of these important facts biochemists in America (Alsberg and Folin; Chas. E. Simon; Wolff and Shaffer) have conspicuously contributed.

**Diagnosis.**—Cystinuria is, as far as we know, a *congenital anomaly* of metabolism. It may be Mendelian in character, for in a number of instances a *family* appearance and a *hereditary* occurrence have been noted.

The *discovery* of cystinuria is usually accidental, except in the cases in which cystin calculi exist. As cystinuria alone causes no symptoms, many cases are doubtless overlooked. In one case of nephrolithiasis in a cystinuric, *urticaria* accompanied the attacks of renal colic; it has been suggested that this may depend upon the *cystinemia;* indeed, it is asserted that, in the case reported, a cystin crystal was observed microscopically in a specimen of the blood!

The cystin excreted daily in the urine in cystinuria may amount to a gram or more. The amount is increased if the diet contain an excess of protein (Williams and Wolff), and diminished if the diet be reduced in protein to minimal amounts (0.8-0.9 g. protein per kg. of body weight). The kind of protein eaten matters but little since all proteins contain arginin, which in turn contains the cystin.

An attempt has been made in a cystinuric to convert the cystin in intermediary metabolism into *taurin* (to be eliminated in the bile) by administering sodium chlorid (Simon and Campbell), but apparently without success; since in animal experiments taurin is thus formed, the method is worthy of further trial.

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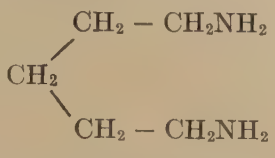
[For other references, see Part IX.]

## 4. The Diamino-acid Diathesis and Diaminuria

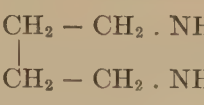
Proteins contain three diamino-acids:

(1) *Histidin* (=Imidazol-$^{\alpha}$-amino-propionic acid).
(2) *Lysin* (=$^{\alpha, \epsilon}$-Diamino-$^{\beta}$-Dithiolactylic acid).
(3) *Arginin* (=$^{\delta}$-Guanido-$^{\alpha}$-amino-n-valerianic acid).

Of these, *lysin* and *arginin*, in certain conditions (among them, the cystin diathesis), instead of being normally catabolized, may, in part, be converted into certain *diamins*, and excreted as such in the urine (sometimes, also, in the feces). Thus a diamino-acid $CH_2 - CH \cdot NH_2 \cdot COOH$ in lysin, by losing a $CO_2$ group, gives rise to *pentamethylendiamin* (= *cadaverin*).



and a diamino-acid $NH_2.C(NH) - NH.CH_2 - (CH_2)_2.CH.NH_2 - COOH$ in arginin by losing a urea-residue, gives rise to *tetramethylendiamin* (= *putrescin*)



In malaria, and in certain gastro-intestinal disorders, cadaverin and putrescin have been found in the feces, though absent from the urine.

As far as we know, no symptoms arise from these anomalies of metabolism. The condition is diagnosed by finding the diamins in the urine, or in the feces, or in both.

For the method of demonstrating the presence of these diamins, special texts may be consulted.

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# D. The Polyurias Other Than Diabetes mellitus

By polyuria is meant the excretion of a larger amount of water than usual by the kidneys.

## 1. Polyuria Following Copious Water Drinking

Ordinarily, an excessive water intake is compensated for, promptly, by an increased amount of urine (*polyuria*), rather than by increase in output by the skin and by the expired air.

Prerequisites for such a polyuria following copious drinking of water are (1) that the needs of the tissues for water are already satisfied, and (2) that the circulatory apparatus (general; portal) is in a normal state. A patient suffering from the retention of NaCl in his tissues (large white kidney), from cardiac decompensation, or from cirrhosis of the liver (portal obstruction) may, if he drink abundantly, instead of secreting more urine, store the extra water, at once, in his subcutaneous tissues, or in his peritoneal cavity (ascites), increasing his body weight correspondingly.

The increase of total N in the urine of the diuresis following a large water intake is due merely to the "washing out" of urea and does not indicate any increase in protein metabolism.

## 2. Polyurias During Compensatory Processes and In Convalescence

In a number of "temporary polyurias," the urine has a *high* specific gravity owing to the washing out of NaCl and urea that has accumulated during a preceding period of oliguria; as examples, may be cited the polyurias following restoration of compensation in cardiac failure or in renal incompetency, and that occurring in convalescence from typhoid fever and other acute diseases (convalescence-polyuria). In the transitory (vasomotor) polyurias accompanying attacks of migraine, epilepsy or hysteria, the specific gravity of the urine may be *low*.

The oligurias and polyurias accompanying cardiac and renal disease need not be described here. The polyuria of diabetes mellitus is described in connection with that disease.

Certain chronic polyurias in which the urine is free from sugar ("insipid" to taste), and in which no demonstrable anatomical changes need be present in the kidneys, are dealt with below, under the heading "diabetes insipidus."

## 3. Diabetes insipidus

### (*a*) *Classification*

Under this term, which designates a "syndrome" rather than a single disease entity, are included a number of conditions, characterized by the excretion, over a long period, of a large amount of urine of low specific

gravity, the kidneys being (anatomically) intact. These conditions may be conveniently divided into two great groups:

(1) *"Idiopathic" diabetes insipidus,* due to a functional disturbance of the kidneys that makes them incapable of secreting a concentrated urine.

(2) *"Symptomatic" diabetes insipidus,* in which there is no functional insufficiency of the kidneys, the polyuria being secondary to a primary (chronic) polydipsia.

### (*b*) *"Idiopathic" Diabetes insipidus*

The functional disturbances of the kidneys in cases falling in the category of *idiopathic diabetes insipidus* have been carefully studied by Eric Meyer. A normal person with healthy kidneys, when placed upon a standard diet of constant content in water, nitrogen and salts, will, in a few days, pass a urine fairly constant both in amount and in total (24 hours) concentration. If to the standard diet of this normal person, more protein or NaCl be added, the extra N, or NaCl, tends to be eliminated quickly, the 24 hours' urine increasing in concentration, and varying but little in amount. When protein and NaCl are added to the standard diet of a patient with idiopathic diabetes insipidus, however, he reacts in an entirely different way; the 24 hours' urine increases markedly in amount and only very slightly if at all in total concentration; the extra N or NaCl is eliminated by means of an increased water-excretion, the specific gravity remaining unchanged (compare the "hyposthenuria" in certain renal diseases in Part X). It is to be noted that we have to deal with the total concentration of the urine, not with its content in any single solid substance; *it is the osmotic functional capacity that is involved,* not an elective secondary function for any single solid or group of solids!

### (*c*) *Symptomatic Diabetes insipidus*

In symptomatic diabetes insipidus, due to primary polydipsia, this inability to secrete a concentrated urine is not present. An increase of the protein or salt intake or a reduction in the water intake is followed by an increased concentration of the urine. Such primary chronic polydipsias with chronic polyuria occur most often in psychopaths (M. Reichardt).

### (*d*) *Diabetes insipidus of Cerebral Origin*

Recently, a flood of light has been thrown upon the idiopathic cases of diabetes insipidus by studies bearing upon the functions of the hypophysis cerebri. After Schäfer and his collaborators had demonstrated the remarkable diuretic effects following upon injection of extracts of the pars intermedia of the hypophysis into animals, attention was called by Frank to

the frequency, in human cases of diabetes insipidus, of symptoms pointing to involvement of the hypophysis. In reported cases, *bitemporal hemianopsia* has several times been mentioned; sometimes an accompanying *acromegaly* or a *dystrophia adiposogenitalis* has pointed to hypophyseal disease; and a *meningitis basilaris syphilitica* has not infrequently preceded the onset of the symptoms of diabetes insipidus (Oppenheim; Nonne). In a recent case, diabetes insipidus followed a *carcinoma-metastasis in the posterior lobe* of the hypophysis, where it could easily, by irritation, have excited an over-function of the intact pars intermedia (Simmonds). The tendency at present is to attribute all the cases of so-called *cerebral diabetes insipidus* to hypophyseal involvement (direct or indirect), and, accordingly, to look upon idiopathic diabetes insipidus as one of the diseases of a gland of internal secretion. Whether this internal secretion of the pars intermedia acts directly upon the secreting elements of the kidneys, or indirectly through stimulation (or inhibition) of the autonomic nerves governing renal secretion, remains to be determined; in the latter event, other pathological irritations in autonomic domains might conceivably cause a true diabetes insipidus, and Steiger (1912) has reported a case that he interprets in this way.

### (*e*) *Diabetes insipidus as a Family Disease*

In rare instances the idiopathic disease may occur in *families* through many generations (Weil). In one family, followed through five generations, 35 out of 220 members showed the symptoms; the polyuria and the polydipsia were manifest even in childhood; three of those affected lived to a ripe old age (83 years; 87 years; 92 years!), being otherwise perfectly healthy.

### (*f*) *Symptoms of Diabetes insipidus*

The two striking symptoms of diabetes insipidus are the *polyuria* and the *polydipsia*. Five to ten liters of urine in the 24 hours are common amounts; in one instance, an amount as great as 43 liters of urine was passed in 24 hours! The *specific gravity* of the urine is very low (1.002-1.005), too low to be registered accurately in the ordinary way; for exact determination, a pyknometer should be used. The *freezing-point lowering* of the urine ( $\Delta$ ) is much higher than normal, varying from — 0.2 to — 0.4. *Nycturia* is common.

Reduction of the water intake in the idiopathic cases to 5 liters may be fairly well borne, but greater reduction often leads to severe discomfort (extreme thirst, restlessness, tachycardia, headache) and sometimes to real danger (retention of urinary solids). Contrary to what might be expected, the polydipsia in diabetes insipidus does not lead to heart hypertrophy or to arterial hypertension. As long as sufficient water is drunk, the daily output of total solids in the urine remains normal.

### (*g*) *Diagnosis of Diabetes insipidus*

The distinction between the idiopathic and the symptomatic group of cases is easy (See above). In every case, the capacity of the kidneys to secrete a concentrated urine should be tested. Polyurias due to other causes (nephritis; convalescence) are easily ruled out.

In view of our newer knowledge of the pathogenesis of idiopathic cases, symptoms of hypophyseal disease, or of basilar meningitis (lues), should always be sought for. In this connection, x-ray examinations of the sella turcica, the Wassermann test, and determinations of the carbohydrate tolerance may be helpful.

In the hereditary cases, a genealogical record should be kept.

The diagnosis should extend also to a determination of the degree of reduction of the water intake compatible with safety (sufficient elimination of urinary solids) when the diet has been arranged so as to lower the osmotic demands made upon the kidney (salt-poor diet; avoidance of protein excess).

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# E. Diabetes mellitus

## 1. Introduction

### (a) *Conception of the Malady*

Diabetes mellitus is a disturbance of metabolism in which d-glucose cannot be utilized in the normal way; owing to this, a patient on an ordinary diet develops a hyperglycemia and excrete d-glucose in the urine either permanently or, at least, over long periods.

Temporary glycosurias (alimentary, piqûre-, toxic, adrenalin-, thyroid-, hypophyseal, phlorhizin-) are, by custom, kept separate from the more permanent glycosuria of diabetes mellitus. Among the experimental glycosurias, that following total extirpation of the pancreas in dogs (v. Mering, Minkowski) most closely resembles spontaneous human diabetes in its severest forms.

### (b) *Diabetogenous Organs*

Both human pathology and animal experimentation support the view that diabetes mellitus is no unity, for prolonged glycosuria may have its origin in disease of any one of several "diabetogenous" organs. Most often, the *pancreas* seems to be responsible ("pancreatic diabetes"), but the *kidney* ("renal diabetes"), the *central nervous system* (piqûre diabetes"), the *chromaffin system,* the *liver,* the *thyroid,* and the *hypophysis* may also, apparently, act as diabetogenous organs. I shall not be surprised if further studies show what we now speak of as the activities of diabetogenous organs are only contributing influences, the fundamental factor in the disease being a defect in the enzyme producing mechanism in all the cells that split d-glucose.

## 2. The Metabolism in Diabetes mellitus

### (a) *Metabolism of the Carbohydrates in Diabetes mellitus*

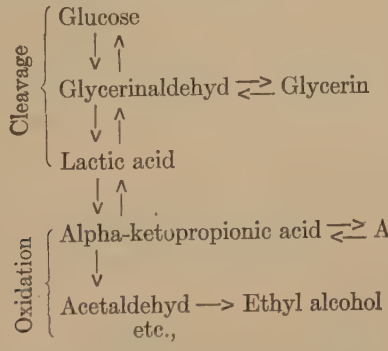
The *normal metabolism of carbohydrates* has already been dealt with. We have seen that d-glucose may be formed in the body not only from the carbohy-

drates of the food (starch, sugars) but also by a process known as *gluconeogeny* from substances other than carbohydrates, especially from (1) certain of the constituent amino-acids of proteins, notably glycocoll, alanin, aspartic acid and glutamic acid), and (2) glycerin. It is possible that sugar may be formed from the higher acids of fat also, though this is still disputed. In normal life, sugar is formed from protein only exceptionally, but in diabetes large quantities of sugar may thus arise. On the other hand, even in diabetes, sugar is never formed from alcohol, nor from those amino-acids of proteins that give rise to oxybutyric acid, viz.: leucin, phenylalanin, and tyrosin. It is the liver that converts other hexoses, as well as the amino-acids of proteins, into glucose; and it is this organ that polymerizes glucose into glycogen and stores it up, to be given off again ("mobilized") as glucose, when required to maintain the normal glucose-content of the blood. Undoubtedly, the liver must be regarded as the central carbohydrate "warehouse" of the body.

The "mobilization" of glucose (conversion of glycogen into glucose in the liver with passage into the blood) seems to be an enzymatic process under the control of the vegetative nervous system, being favored by epinephrin stimulation of the sympathetic system and inhibited by stimulation of the vagus by a hormone derived from the internal secretion of the pancreas; this hormone passes from the pancreas through the lymph vessels into the thoracic duct and thence into the left subclavian vein.

In all forms of diabetes (except the renal form due to phloridzin) there is an excess of glucose in the blood **(hyperglycemia)**, often as much as 0.5 per cent, which is three or four times the normal amount (0.8-1.2 per cent). In *phloridzin-diabetes,* on the other hand, the glucose-content of the blood may sink as low as 0.05 per cent.

In the normal catabolism of the sugar brought by the blood to the tissues (especially the muscles), the glucose first undergoes *cleavage*—it is "split"; only subsequently to this cleavage does it undergo *oxidation.* Just what stages are gone through in these processes of cleavage and oxidation, we do not yet know. The following scheme has been suggested as probable, the arrows in both directions indicating that the processes are reversible:




the ultimate products being carbon dioxid and water.

One theory is that in human diabetes (and in experimental pancreatic diabetes in dogs), the fundamental disturbance is a *loss (or impairment) of the power to split glucose* (rather than a loss of power to oxidize the cleavage prod-

ucts). As we have seen, Woodyatt and others think that the failure of cleavage may be a defect in dissociation (see Chemistry of the Sugars).

According to a second view, which numbers many adherents including so distinguished an investigator as v. Noorden, the essence of the disease consists in a *too rapid mobilization of the sugar* in the liver with resulting hyperglycemia and glycosuria. Still other theories have been referred to under the chemistry of the carbohydrates (*q. v.*).

Since diabetes mellitus is certainly no unity, it may very well be that some cases depend chiefly upon a disturbance in one direction, others upon a disturbance chiefly in another. A decision regarding the validity of these theories must await the results of further inquiries.

An enormous amount of work has been done on metabolism in diabetes, too much of it unfortunately by methods that will not stand the test of rigid criticism. Only the outstanding results will be referred to here. To follow the carbohydrate metabolism in diabetes accurately, it is necessary to know the food eaten and to determine the quantity (in grams) of sugar excreted each twenty-four hours. The degree of glycosuria depends, in a given case, chiefly on the food eaten; it is influenced, not only by foods containing carbohydrates, but also by carbohydrate-free foods (proteins, fat). It is a well-established fact that the liver and muscles, in all except the mildest cases of diabetes, no longer store up glycogen.

In mild cases, milk sugar, levulose, and inulin may be better borne than d-glucose, but in severer cases these sugars, like d-glucose, cannot be utilized at all. The foods containing polymeres of d-glucose (*e. g.*, starch, dextrin), influence the glycosuria chiefly according to the amount of carbohydrate they contain; the form has, however, some influence, since the same quantity of carbohydrate taken as oatmeal, potato, or banana seems to be better borne than when taken as bread. Experience with the oatmeal cure indicates that, in some cases, large amounts of carbohydrates without any meat can, for a time, be better utilized than small amounts of bread given with meat and eggs. Alcohol and fat in the diet do not, as a rule, increase a glycosuria, though I have recently studied two cases in which the urine could not be kept sugar-free unless the fat ration was kept low. Protein in excess increases the glycosuria, egg and vegetable protein less than that from milk or meat.

When the power to utilize glucose is only moderately involved (mild cases of diabetes), the glycosuria for a given carbohydrate intake may be lessened by *muscular exercise.* In severe human diabetes, and in diabetic dogs (as shown by treadmill experiments), muscular exercise does not lessen the sugar output; on the contrary, it may increase it.

*Physical traumata* (accidents, surgical operations) and *psychic influences* (worry, sorrow, mental strain) increase the glycosuria.

In estimating the degree of glycosuria, and especially in trying to determine the amount of oxybutyric acid in the urine after fermentation of the sugar, the possibility of the presence of levorotary *glycuronic acid* should always be kept in mind; it is sometimes present in large amounts in the urine of diabetics.

### (*b*) *The Protein Metabolism in Diabetes mellitus*

The *protein metabolism* in diabetes mellitus is also full of interest. The high nitrogen output in the urine is due chiefly to the large protein intake (polyphagia, excessive meat eating). A part of it, when the patient is emaciating, is doubtless due to burning of proteins of the body musculature. Provided a patient can digest fats well, it is usually possible, however, by careful regulation of the diet to maintain nitrogenous equilibrium even with a relatively low protein intake; indeed, the physician may succeed in rebuilding some of the lost muscle substance, especially if the carbohydrate tolerance be gradually increased. These studies have gone far to modify the dietary of diabetics in recent years, so that at present there is a strong reaction against the excessive meat intake formerly prescribed. That a toxic disintegration of protein sometimes occurs in diabetes, cannot be denied; it requires further study.

The degradation of protein in diabetes appears to follow normal paths; the fact that part of the N appears in the urine as $NH_3$ instead of as urea, in cases with acidosis, is simply due to the union of $NH_3$ with organic acids; this prevents its further synthesis to urea.

### (*c*) *The Fat Metabolism in Diabetes mellitus*

The importance of *fat metabolism* in diabetes grows as our knowledge of the disease progresses. In the degradation of fat in diabetes, no abnormal path is followed. Down as far as the stage of butyric acid all cleavages and oxidations proceed normally, but in the absence of a normal utilization of carbohydrates in metabolism, the substances resulting from the cleavage of the higher fatty acids (stearin, palmitin, etc.) of fat, just before they reach the butyric acid stage, are transformed into oxybutyric acid and diacetic acid and are not further oxidized. These organic acids also arise from certain of the amino-acids (leucin, tyrosin, phenylalanin), formed on the splitting of protein. Thus derivatives of both fats and proteins are mother substances of the "acetone bodies," both are "ketogenous" constituents of the food. It is estimated that 100 g. of neutral fat can give rise to about 36 g. of oxybutyric acid, 100 g. of protein to a little less. The liver appears to be the chief site of formation of these organic acids; whether other organs also participate, we do not yet know.

The relation of the three acetone bodies to one another has already been discussed (see above); it is clear if the structural formulae be examined:

$CH_3 - CHOH - CH_2 - COOH$ = Beta-oxybutyric acid.
$CH_3 - CO - CH_2 - COOH$ = Diacetic acid (Aceto-acetic acid).
$CH_3 - CO - CH_3$ = Acetone (Dimethylketone).

It is probable that oxybutyric acid is the primary product, and that it is oxidized to diacetic acid; sometimes, however, diacetic acid is reduced to oxybutyric acid (Dakin). Acetone is a cleavage product of diacetic acid.

The accumulation of these organic acids in the body is called **acidosis**; their excretion in the urine is spoken of as **ketonuria** or **diaceturia.** In marked acidosis, acetone is given off in the breath, giving rise to the characteristic fruity odor, so important for diagnosis. The kidneys excrete the ammonium salts of oxybutyric acid and diacetic acid, but little or no acetone; when acetone is present in the urine, it arises from diacetic acid after it is excreted.

Acetone bodies are formed in normal metabolism, but do not accumulate as long as carbohydrates are split and oxidized in normal amounts. In this sense "fats are burned in the carbohydrate fire." In the fasting body, or on an exclusive meat diet, the normal organism keeps the acidosis within bounds, rarely excreting more than 10-15 g. of acetone bodies, owing to the fact that it still burns the sugar made in the body from protein. Similarly, in mild diabetes, there is no acidosis as long as the body is able to burn 40 to 80 g. of glucose. But in the severer forms of diabetes (and in mild forms on carbohydrate-free diet) the acidosis may be marked, the 24 hours' urine containing 30 to 60 g. of acetone bodies or more. The presence of diacetic acid in the urine can be recognized qualitatively by the ferric chlorid test, but this color reaction is of but little value for quantitative estimation. When no sodium bicarbonate is being administered, the determination of the ammonia output gives an approximate idea of the degree of ketonuria. One of the best practical guides to the degree of acidosis existing is to determine the amount of $NaHCO_3$ necessary to render the urine alkaline or amphoteric, as follows:

Normally, 5-10 g. $NaHCO_3$ are required.
In mild acidosis, 20 g. (= less than 15 g. acid).
In severer acidosis, 30 to 40 g. (= 20-30 g. acid).
In extreme acidosis, 40 g. or more (= 30-40 g. acid).
In coma (when excreted), often non-neutralizable (= 50-150 g. acid).

The amount of beta-oxybutyric acid present varies from twice to seven times the amount of diacetic acid in the urine. Acidosis causes increased depth of respiration (the minute volume of respired air is increased); a delicate test for acidosis is the determination of the diminution of the **$CO_2$-tension of the venous blood** in diabetes, since, in coma, the $CO_2$-content may fall from 40 per cent to 15 per cent or even lower. To judge the significance of the acidosis in a given case, observations over a considerable period, with careful control of the diet, are essential.

In fighting acidosis *directly,* we try to favor the burning of glucose, *i. e.,* we try to increase the carbohydrate tolerance. Thus, carbohydrates if they burn are "antiketogenous" in influence. Alcohol has an antiketonuric effect, even in severe diabetes; it may be worth while to try the effects of leucin and tyrosin.

In *indirectly* fighting the acidosis by neutralization of the acids, thus

combating further withdrawal of alkalis from the cells, and accelerating the excretion of the acids in the urine, nothing is more successful than the administration of sodium bicarbonate in quantities sufficient to keep the urine amphoteric to litmus. A patient will often require (and may tolerate well) 30 to 40 g. of $NaHCO_3$ daily for months. If the onset of coma threaten, a teaspoonful dissolved in water may be given every half hour until the urine is alkaline; if coma have already appeared, it is advisable to give a liter of a 4 per cent. solution of $NaHCO_3$ intravenously (never subcutaneously). Since the development of the starvation treatment of diabetes by Allen, it has become necessary to revise, to some extent, our former ideas with regard to diabetic acidosis and its management (see below).

The *lipemia* of severe diabetes has already been referred to. It does not appear to be due to any disturbance in the cleavage and oxidation of fat, but depends upon an unexplained retention of food fat in the blood.

### (*d*) *The Mineral Metabolism in Diabetes mellitus*

The *metabolism of water and of inorganic substances* (*constituents of ash*) in diabetes mellitus has been the object of a number of careful studies.

**Water.**—The *polyuria* as a rule keeps pace with the sugar output; thus if 2 liters of urine be passed (sp. gr. 1.028-1.030), the sugar-content will be found to be 2-3 per cent.; if 5 liters be passed (sp. gr. 1.030-1.035), the sugar-content is 5-7 per cent.; even when 6-10 liters are passed, the urine will rarely contain over 6-10 per cent of sugar (sp. gr. 1.030-1.042). In atypical cases, the amount of urine may be normal and yet 2 to 5 per cent of sugar may be present (*diabetes decipiens*); occasionally there is polyuria with low sp. gr. (1.005) with less than 1 per cent of sugar. Strange variations in the water metabolism—sometimes excessive loss of water with drying of the tissues, sometimes retention of water with edema (especially on $NaHCO_3$ administration or during oatmeal cures)—are not infrequently met with, and account for sudden, surprising losses or increases in the body weight.

**Ca, Mg, NaCl, S, P.**—In acidosis, Ca and Mg may be rapidly withdrawn from the body. The large amounts of *sodium chlorid* excreted are usually due to the polyphagia, the excessive amounts of *sulphur* and *phosphorus,* to the large protein intake.

### (*e*) *The Total Metabolism in Diabetes mellitus*

As to the *total metabolism* (*calories*) in diabetes we already have some reliable information. Especially accurate is that given us by Benedict and Joslin as a result of their studies in the Carnegie Institute for the Study of Nutrition; they prove that the conclusions arrived at earlier by

less exact studies were in the main correct. The *emaciation* met with early in diabetes is due to the glycosuria; every 100 g. of sugar in the urine corresponds to a loss of 400 calories. A patient of Fuerbringer's, a woman weighing 43 kg., during nine days' observation, excreted, on the average, daily, 14 liters of urine containing 930 g. sugar and 64 g. nitrogen! In emaciating patients, the protein and the fat of the body are gradually consumed. To combat the emaciation, it has been the custom to abolish or diminish the glycosuria by regulating the diet (restriction of carbohydrates and increase of protein and especially of fats). In mild cases of diabetes in which 60 to 80 g. carbohydrate can still be utilized it has been, as a rule, easy to maintain weight and strength. In the severer forms, this has been difficult unless the patient's digestive organs will permit of a large fat intake (150-200 g. daily). Allen believes that in the severer cases, emaciation is necessary and desirable (See below).

The direct calorimetric studies of diabetic patients by Benedict and Joslin show that, in mild cases, the total metabolism shows no essential deviation from the normal. In severe cases, however, the amount of oxygen used *per kilogram* of body weight is increased, on the average, about 20 per cent. The *absolute amount of food needed,* however, is not increased, since this increase of metabolism per kilogram is compensated for by the smaller weight of the emaciated patient; thus the diabetic patient weighing 60 *kg.* showed a total (absolute) metabolism exactly equivalent to that of a healthy person weighing 68 *kg.* under the same conditions.

There is some evidence to show that there may, at times, be a diminution in total metabolism in patients with severe diabetes who have become accustomed to a very strict diet (Weintraud, Magnus-Levy); and it is also probable that the total metabolism is increased in certain polyphagic patients in whom emaciation progresses despite a high figure for the amount of oxygen used per kilogram (Rolly). Such unusual cases require further study. Preceding the starvation treatment of Allen, it was believed that the most important practical point was to give a diet rich in fat, moderate in protein and restricted in carbohydrate to correspond to tolerance.

## 3. Ordinary Clinical Studies of Diabetes mellitus

### (*a*) *Etiology*

The causes of diabetes are as yet unknown. *Heredity* is an important factor; the disease exists among ancestors, or sibs, in at least 20 per cent of the cases. The disease is more frequent after the *age* of 40. It affects preferably *"good livers,"* and is especially common among *Jews.* The symptoms often develop after an *infection,* or a *trauma* (physical or psychic). *Gout, obesity,* and *arteriosclerosis* are common in diabetic families. *Conjugal diabetes* (1 to 3 per cent of all diabetes cases) hints at environmental influences in common.

### (*b*) *Symptoms of Diabetes mellitus*

The glycosuria is discovered earlier now than formerly owing to the routine examination of the urine in all clinical work and in life insurance tests. The physician's suspicions should be aroused when patients complain of increased *hunger* and *thirst, polyuria, nycturia,* unexplained

Fig. 640.—Diabetic Gangrene. (Med. Service, J. H. H.)

*emaciation,* increasing *weakness, furunculosis* or *carbuncles,* rapid *caries of teeth,* or loss of teeth from *pyorrhea, pruritus,* bilateral *neuralgias,* especially sciatic, *cramps* in the calves of the legs, *impotence, balanitis,* or early *cataract.* At the beginning of the disease, the only symptoms may be a *glycosuria,* accidentally discovered. Diabetic *gangrene* occurs most often in the milder chronic cases; it is sometimes though not always preceded by *intermittent claudication.*

The examination of the *blood,* in addition to hyperglycemia, may reveal a positive *Brehmer reaction* (reduction of anilin dyes). In some diabetics with acidosis, a high grade of lipemia (1 to 27 per cent of fat in the blood) may exist, the blood fat being rich in lipoids, cholesterin and lecithin. This *diabetic lipemia* seems to be due to defective removal of food fats from the blood with resulting accumulation; the highest grades of lipemia are seen in diabetic coma.

The *urine* in addition to the glycosuria and ketonuria (*vide infra*) often contains albumin; this albumin may be independent of the diabetes, or it may be due directly to a diabetic nephropathy. Older clinicians reported cases in which albuminuria and glycosuria alternated (*diabetes alternans.*)

In the *nervous system,* besides neuralgias (facial, intercostal, sciatic), actual neuritis may occur with anesthesias, paresthesias, loss of knee-kicks (33⅓ per cent of all cases) and skin reflexes, and trophic disturbances (*e. g.,* malum perforans); in some instances, such a peripheral neuritis may at first be mistaken for tabes dorsalis (diabetic pseudotabes). The gravest of all symptoms referable to the nervous system is **diabetic coma** (*coma diabeticum, coma dyspnoeicum*) with its drowsiness deepening to coma, its deep breathing (*"grosse Atmung"* of Kussmaul), and a fruity odor to the breath often preceded by showers of short, broad, delicate casts ("coma casts") in the urine, by increased diaceturia (ferric chlorid test), and by diminished $CO_2$-tension in the venous blood. An occasional patient may recover from diabetic coma through energetic treatment with large quantities of sodium bicarbonate, but the majority die within 24 to 48 hours after the onset of the coma. At least 60 per cent of the deaths in the severer forms of diabetes are due to diabetic coma. One of the most important tasks of the physician is to prevent and combat the acid intoxication leading to coma (dietetic management; efforts to increase carbohydrate tolerance; administration of alkalis).

### (c) *The Course of the Disease*

As a rule, the *onset* is insidious and the *course* chronic. Occasionally, the onset is sudden and the disease severe from the beginning; in such cases death may follow in a few weeks, though, occasionally, a patient with acute onset may get well, or the disease may go over into a chronic form.

It has been found convenient to classify cases in *three groups:* (a) mild, (b) moderately severe, and (c) extremely severe.

In the **mild cases** the glycosuria quickly disappears (3 days) on a carbohydrate-free diet; indeed, the patients may tolerate 40-60-100 g. carbohydrate without glycosuria. Most patients past middle life belong to this group. The carbohydrate tolerance can often be increased by careful management. Patients may live 10 to 20 years or longer; they often die of arteriosclerosis, contracted kidney, or pulmonary tuberculosis. Coma is far less common in them than in the severer cases.

In the **moderately severe cases** there may still be glycosuria after three days of carbohydrate-free diet, though the urine may become sugar-free in two or three weeks even without the intercalation of "fasting days" or "vegetable days." Such cases, on longer observation, may become either milder or more severe. The acidosis is moderate.

In the **extremely severe cases,** the glycosuria persists despite carbohydrate-free diet, and often despite "hunger days" or "vegetable days." The acidosis is severe, owing to the total inability to metabolize carbohydrates. The diabetes of children and of young people (under 25) is often of this severe form; occasionally, the diabetes of more advanced life is also severe. Death from coma is the common ending (60-75 per cent of the cases). Death from "galloping consumption" is also frequent. Even these severe cases can now be made sugar-free by Allen's method (See below).

### (*d*) *Diagnosis of Diabetes mellitus*

#### i. The Glycosuria

After establishing the presence of a glycosuria, and having excluded maltosuria, levulosuria, lactosuria, pentosuria (See Part IX), we must find out whether the glycosuria is "transitory" or "accidental," or the more permanent glycosuria of diabetes mellitus.

*Transitory glycosuria* may be due to any one of many different causes. It may be alimentary. It may follow an apoplectic or an epileptic attack. It occurs also in certain intoxications (morphin; CO) and in acute infections. Occasionally, it complicates gout, Graves's disease or cirrhosis hepatis. Such a transitory glycosuria should not be regarded too lightly; sometimes, at the beginning of a diabetes mellitus, the sugar is absent during certain periods (*diabetes intermittens*).

#### ii. Determination of the Carbohydrate Tolerance

Whenever possible, the *tolerance for carbohydrates* should be determined in patients who exhibit a glycosuria. This is most easily done if the patient will enter a clinic or a nursing-home where the food can, for a couple of weeks, be strictly controlled by a trained nurse, and quantitative sugar determinations made by the physician; it is difficult to manage in the patient's home. Without the determination of the tolerance, we work in the dark in treating diabetic patients.

We may determine the tolerance of a patient for carbohydrates by either one of two methods: (1) after gradual withdrawal of carbohydrate foods; or (2) after sudden and complete withdrawal of all foods (total starvation method).

##### 1. *Tolerance After Gradual Withdrawal of Carbohydrate Foods*

This is the method that, up to very recently, has been generally in vogue among physicians who specialize in diseases of metabolism, and it is the method that until the end of 1914 I have used in my own diagnostic studies. Since 1914, I have used Allen's method.

When applying this method, the patient is placed on an ordinary diet

for a couple of days and the sugar output in an aliquot portion of the total 24 hours' urine determined. He is then placed on a "strict" or "carbohydrate-free" diet (*vide infra*) plus 100 g. white bread (=60 g. carbohydrate) per day for three days. The urine is collected, quantitatively, and its sugar-content for each day recorded.

In *very mild cases,* the urine may, before the third day, become sugar-free; in *cases of medium severity,* the sugar output will fall to 20 g. or 10 g.; while in the *more severe cases,* the sugar output may equal the carbohydrate intake (60 g.) or exceed it.

The patient is now given the "strict" diet plus 60 g. white bread (= 36 g. carbohydrate) for two days, and then "strict" diet plus 30 g. white bread (= 18 g. carbohydrate) for two days. After this, the "strict" diet (carbohydrate-free) is given alone for three or four days. In all except the *severer cases,* the urine becomes sugar-free; if 1 or 2 g. sugar be still excreted, it can often be made to disappear by prescribing a single "fast day" or a "vegetable day" (*q. v.*).

In the *severest cases,* however, sugar will still be excreted (being made in the body from the protein of the food or from the protein of the body itself). In such cases, by cautiously proceeding for several weeks with strict diet, with reduction also of the protein and of the fat, the observance of occasional "fast days" and "vegetable days," with trials, perhaps, of "oatmeal periods," the patient's urine may, sometimes, be made sugar-free.

In the milder cases and in the cases of medium severity, after the urine has been sugar-free for three or four days (on "strict" diet), 20 g. of white bread may be added to the diet every other day until sugar reappears in the urine. The tolerance of the patient in terms of white bread, or in terms of pure carbohydrate (=grams of white bread $\times \frac{6}{10}$) has then been determined.

*While testing the carbohydrate tolerance, sodium bicarbonate should in every case be given when the carbohydrate intake falls below 60 g. In mild cases, 20 g. $NaHCO_3$ should be given daily; in severer cases, 40 g.*

**"Main," "Strict," "Standard" or (So-called!) "Carbohydrate-free" Diet.***

1. *Meat.*—Including fowl, fish, oysters, crabs, clams, sausages, sweetbreads, kidney, brain, but not liver (because of its glycogen-content). Sauces containing flour are of course prohibited. Cooked meat = 25–30 per cent protein; cooked fish = 20 per cent protein.

2. *Eggs.*—(1 hen's egg weighing 50 g. = 6 g. protein + 5 g. fat = 71 calories). The protein content of one egg is the equivalent of that of 20 g. of cooked fish.

3. *Cheese.*—Usually contains 25 per cent protein and from 12 to 75 per cent of fat.

4. *Fats.*—Butter (85-99.5 per cent fat); olive oil (100 per cent fat); fat bacon (90-95 per cent fat); bone marrow.

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[* It is not really carbohydrate-free, for the meats contain a little glycogen and the vegetables from 4 to 6 per cent carbohydrate].

5. *Certain vegetables.*—Spinach, cabbage, sauerkraut, cauliflower, asparagus, young rhubarb, string beans, artichokes, cucumbers, mushrooms; these vegetables may have much butter added, *but no sugar;* they contain traces of carbohydrate (up to 6 per cent). By "thrice boiling" in different waters they can be rendered almost carbohydrate-free.

6. *Certain salads.*—Lettuce, endive, cress, romaine, cucumber, tomato, string bean, asparagus, olives. Oil and vinegar may be added, as well as salt and pepper.

7. *Certain fruits and nuts.*—Young gooseberries, cranberries, blackberries, currants, almonds, hazelnuts, walnuts.

8. *Certain soups.*—Made without flour, though parmesan cheese, roborant or gliadin may be used as a "binder"; thus, bouillon or consommé may contain egg, cut green vegetables, asparagus tips, meat cubes, etc.

9. *Drinks.*—Lemonade (unsweetened), mineral waters, coffee or tea (with saccharin, crystallose, or hediosite to sweeten); Moselle wine, Rhine wine, claret, sherry, whisky, brandy.

**"Accessory" or "Carbohydrate-containing" diet (to be used in prescribed amounts only).**

| | Carbohydrate Content Percentage | Amount in grams. = 20g. White Bread = 12g. Carbohydrate |
|---|---|---|
| White bread | 60 | 20 |
| Coarse black bread | 50 | 22 |
| Zwieback | 70 | 17 |
| Oatmeal | 67 | 18 |
| Rice or macaroni | 70–80 | 15–17 |
| Cocoa | 30 | 40 |
| Potato | 18–20 | 60–70 |
| Turnip | 7–10 | 120–170 |
| Jerusalem artichoke | 15–20 (inulin) | 60–80 |
| Cherries | 12–14 | 80–100 |
| Grapes, plums, peaches, apples, pears. | 10 | 120 |
| Melons, strawberries, raspberries, blackberries | 5 | 240 |
| Milk | 4.8 | 250 |
| Kefir | 2.4 | 500 |
| Cream (thick) | 3 | 400 |
| Beer | 4–5 | 240–300 |
| Oranges | 6 | 200 |

Thus, if a patient were allowed, say 80 g. white bread (=48 g. sugar) he might, if he cared to, substitute therefor:

(1) 44 g. black bread + ½ liter milk, or
(2) 30 g. white bread + 150 g. potato, or
(3) 30 g. rice + ½ liter milk, etc., etc.

**"Fast Day"** (*Naunyn*).—Only water, bouillon, tea, lemonade, and wine or whisky (100 c.c.) are taken for 24 hours.

**"Vegetable Day"** (*v. Noorden*).—Three meals are given, each consisting of 250 g. thrice-cooked vegetables and salads (from "strict" list); to those are added in the 24 hours 4 to 6 eggs, 100 g. butter (or more), a little fat bacon, the yolks of 3-4 eggs, coffee, tea, lemonade, bouillon, and a pint of wine. Two or three such days may follow one another, if desired.

**Tolerance for Particular Carbohydrates.**—In diabetes cases, the "special tolerance" and the "special sensitiveness" for particular carbohydrates, particular proteins and particular fats may have to be tested. Some patients are "protein sensitive," doing better on a low protein ration; others are particularly sensitive to

certain forms of carbohydrate while they are fairly tolerant of others. Hence have arisen the various "carbohydrate cures," including the "rice cure," the "wheat cure," the "potato cure," the "rye cure," and, most important, perhaps, of all, the "oatmeal cure" of v. Noorden.

*The "Oatmeal Cure."*—In severe cases of diabetes mellitus, with high acidosis, as well as in cases of medium severity, the "oatmeal cure" is often well borne and, properly applied, may lead to an increase of the carbohydrate tolerance of the patient. In principle, it consists in giving a large amount of carbohydrate in the form of oatmeal, along with a large fat ration and a small protein ration. Thus, in 24 hours the patient receives:

1. 250 g. oatmeal, or rolled oats (cooked slowly for 2-3 hours).
2. 200-300 g. butter (or butter and bacon).
3. 4-6 eggs (or 50-100 g. vegetable protein, such as gliadin or roborant).
4. 100-150 g. green vegetables (from the "strict" list), or salad.
5. Some alcohol (a pint of hock or 100 c.c. whisky with water).
6. Coffee, tea, lemonade, mineral waters.

Before testing the patient's response to such an oatmeal cure, it is important to prepare him by several days of "strict" diet and one or two "vegetables days" in order to reduce the glycosuria and the hyperglycemia. He is then given from two to four "oatmeal days," followed by one or two "vegetable days"; after this, a few days of "standard diet" are permitted. When well borne, two, three, or even more of such cycles may be permitted. In many cases, acidosis diminishes markedly, and tolerance improves greatly. In some of the grave cases, no benefit results; the sugar output stays high (120-150 g.), the acidosis is not lessened, nor does the general condition improve; here the outlook is grave, though, even in such cases, remarkably good results can sometimes be obtained by the starvation method (See below). One cannot prophesy beforehand how a patient will respond; the trial must be made to find out. A satisfactory explanation of the mode of action of the oatmeal cure is still lacking.

### 2. *Tolerance After Sudden and Complete Withdrawal of all Foods (Starvation-Method)*

This method, worked out by Allen (1914-1915), is now under trial. Allen's results have been so favorable that I have been led to try his method in a number of instances, and thus far I am much impressed with the good results obtainable. Joslin, of Boston, has also tried the method in his large diabetic practice, and he, also, feels that a distinct step forward in tolerance testing and in the treatment of diabetes mellitus has been made.

After having made a thorough review of the bibliography of diabetes mellitus, Frederick M. Allen undertook the study of experimental diabetes and its treatment in laboratory animals, and arrived at certain conclusions regarding the testing of carbohydrate tolerance and the starvation treatment of diabetes, which, since 1914, he has been applying also to human beings.

In the bibliography, Allen was impressed by (1) Rollo's limitation of diabetic patients to animal food (1796); (2) Bouchardat and Cantani's restriction of a harmful excess of protein, and their employment of green vegetables in diabetes; (3) Naunyn's influence in favor of the restriction of protein and the observance of occasional fast days in diabetes; (4) Stadelmann's theory of acid poisoning as the cause of diabetic coma and his inauguration of the alkali treatment of

acidosis; (5) the introduction, in 1903, by von Noorden, of the oatmeal cure and his use of fast days and vegetable days ("metabolic Sundays") (a) as a preparation for his oatmeal treatment by increasing the tolerance and (b) to prevent coma; and (6) the crude but interesting attempts of Guelpa to treat diabetes by fasting and purgation, on the ground that the disorder is due to an auto-intoxication.

Allen favors the view that, in diabetes, there is a loss of power to utilize sugar, not a mere acceleration of sugar formation. He also thinks it established that the internal function of the pancreas makes possible, in some way, the utilization of sugar by the tissues, but he sees no valid proof in the bibliography for the view that the adrenals oppose this function of the pancreas, or that the pancreas inhibits sugar formation or opposes the adrenals in any way. Allen has been favorably impressed by the simple objective description of diabetes given by Macleod at the beginning of his book, in which it is stated that diabetes appears, at first, as a weakened function of carbohydrate metabolism; that, subsequently, there is a weakening of the function of protein metabolism, and that, finally, in the severer cases, there is also imperfect metabolism of fat. He thinks it desirable that we should avoid looking upon diabetes as a progressive fatal disease, since, thus far, an inherent downward tendency has not been definitely demonstrated. If we consider the disorder rather as a simple weakness of a bodily function, without inherent downward tendency, we may, he thinks, keep our patients, if they are obedient, from going downhill simply by preventing them from over-taxing the weakened function.

With these conceptions in mind, Allen worked out a method of testing carbohydrate tolerance in experimental diabetes and of treating this diabetes in animals (1914). On removing nine-tenths of a dog's pancreas, he found that, if he tried to keep the dog fat and to satisfy its large appetite, the animal went steadily downhill for several months and died in extreme cachexia. He further found that he could stop the glycosuria in the dog by making the animal fast, and afterwards restricting the food intake to a low diet, large enough to support life, though not large enough to cause glycosuria. The animal remained thin, but was strong and lively, developed no cachexia, and showed no signs of downward tendency.

In 1915, Allen published an article in which he reports the management of diabetic human beings on the same principles. His **first step** is *to make the patient fast until the glycosuria ceases, and for 24 or 48 hours longer.* The ketonuria declines precipitately, and quickly approximates that that would be shown by a normal person under similar conditions as regards diet. Allen's aim is to keep the ketonuria constantly down to such a level. He finds that simple fasting suffices for his purposes, but as alcohol is a food that does not cause glycosuria and may perhaps diminish ketonuria, he gives it during the fast, especially in the severer cases, where coma might reasonably, from our knowledge of diabetes, be feared. He also administers sodium bicarbonate for the first few days, but then gives up its use, since its continuance may cause the diaceturia to continue longer than it otherwise would.

After the urine of the fasting patient has been sugar-free for from

24 to 48 hours, the **second step** is undertaken, namely, *the beginning of feeding, very slowly and cautiously,* but not according to any fixed program, since it is desirable to individualize the diet to suit the special need of the patient under observation. One requirement only is insisted upon, and that is that *the patient shall remain free from both glycosuria and acidosis.* The appearance of even a trace of sugar in the urine is the signal for a fast day, either with, or without, alcohol.

Though the original fast, by which the urine is first made sugar-free, may last anywhere from two to ten days, Allen asserts that, subsequently, no fast need last longer than a single day.

In the diet, attention has to be paid to the *carbohydrate intake,* the *protein intake,* the *fat intake,* and the *bulk* of the food. He first tests the **carbohydrate tolerance.** Carbohydrate may be the first food to be administered after the fasting. Allen usually begins by allowing vegetables, making use of Joslin's convenient classification of these on the basis of their carbohydrate content. On the first day after the fast, he usually allows 200 grams of vegetables of the 5 and 6 per cent classes. Subsequently, he increases the amount of vegetables, day by day, until a trace of sugar appears in the urine; then a fast day at once is prescribed. The content of the vegetables in carbohydrate being known, the carbohydrate tolerance has thus been determined. In the meantime, the acidosis will, as a rule, have been reduced to a level corresponding to that of a normal human being on a similar diet.

Having tested the carbohydrate tolerance in this way, Allen proceeds to test the **protein tolerance.** On the first day of this test, he gives one or two eggs, perhaps, and nothing else; subsequently, day by day, more protein, usually in the form of eggs and meat, is added to the diet, until glycosuria appears, or until a sufficient protein ration has been reached. In this way, the amount of protein that can be taken without causing glycosuria is determined, and the protein loss of the body is overcome as quickly as possible.

The **fat tolerance** may also have to be determined in the severe cases (See below).

A certain **bulk** to the diet is necessary to prevent constipation and to satisfy the patient's need for a feeling of fullness. To give bulk, the green vegetables recommended serve admirably. They may be used raw, or they may be cooked by steam, or in boiling water, the water being subsequently evaporated so that the carbohydrate and salts remain in the vegetables. This, at any rate, has been found satisfactory in the milder cases. In the severer cases, Allen finds that even green vegetables, thus prepared, cannot be eaten without causing glycosuria. He cites an instance in which a young girl developed glycosuria when she received nothing except 100 grams of celery and lettuce in 24 hours. In such severe cases, the vegetables may be boiled in three successive waters and all the water thrown

away. Removal of nearly all the carbohydrate is thus made possible. Such thrice cooked vegetables are said to be palatable and, when eaten, they do not cause glycosuria.

The patients, of course, lose weight at the beginning of the application of this method, but Allen believes that this **loss of weight** is beneficial. Later on, after the carbohydrate tolerance has been determined, and the glycosuria and acidosis abolished, the patient is permitted to gain weight as long as he can do so without developing glycosuria and without increase of the acidosis.

Allen makes the statement that "the attempt to put on weight according to the time-honored traditions of diabetic treatment is one of the surest ways of bringing back all the symptoms and sending the patient downhill." Accordingly, in severe cases of diabetes mellitus, a **restriction of all classes of food is necessary,** and the tolerance of each patient for each particular class of foods must be determined. Allen permits some *carbohydrate,* if possible, but he never gives it except safely below the limit of carbohydrate tolerance. He finds also that the intake of *protein* must be kept fairly low, sometimes very low. When the protein tolerance is found to be exceedingly low, he excludes all carbohydrate from the diet, and then permits as much protein as is possible without causing glycosuria. He states that every patient thus far studied can tolerate his necessary protein minimum, and that glycosuria will not appear unless this indispensable protein minimum be exceeded. One of the astonishing statements made by Allen concerns the intake of *fat.* Hitherto fat has been considered not only safe, but necessary, in the diabetic dietary. Though Allen mentions that he has never seen glycosuria occur from a pure fat diet, he has nevertheless observed patients whose urine remained constantly sugar-free on a given diet, who began to put out sugar and an increased quantity of acetone bodies as soon as butter, or olive oil, was added to the diet.

Allen's experience, owing to the short time that had elapsed since he began to study patients in the manner described before making his report, included, up to February, 1915, some 27 cases, most of them of very severe type. The longest observation of any one patient up to the time of the writing of this article was nine months. The results he has reported are certainly very gratifying. The method used leads to the improvement of many patients who do not do well on the treatment formerly in use; and, further, even the patients who respond well to the ordinary methods can now improve much more quickly. The author makes no claim, of course, regarding permanent results, since these have yet to be demonstrated; time alone can give us information regarding the ultimate value of his method.

Allen emphasizes, with right, the separation of what he calls the *scientific factor* from the *human factor* in judging of the results of any method of treatment

in diabetes. The **scientific factor** is concerned with the value of the treatment under ideal conditions. It is his belief that "it gives the vision of a diabetes in which there is no glycosuria, no acidosis, no use for alkalis or other drugs, no complications, no gangrene, no downward progress, no coma, no death." Whether the future will justify this roseate view or not will depend, he thinks, largely upon whether there is, or is not, an inherent downward tendency in diabetes. He has hoped that by a protective therapy, such as he has been using, the tolerance for carbohydrates might improve markedly, even in very severe cases. Thus far, this hope seems to have met with disappointment, though a gain in tolerance may be met with in the milder cases. Allen believes that severe cases of diabetes mellitus ought not to be permitted to develop. He thinks that if the patients could come, near the outset of their trouble, under the care of practitioners who would stop the glycosuria and the ketonuria, the disease need not progress. Though this view may hold good for many cases, it is possible that progressive lesions do occur in some cases of diabetes, which cannot be arrested even by the protective therapy. It would seem right, however, to impress the great mass of general practitioners, who see diabetes in the early stages, with the importance of applying efficient methods of diagnosis and treatment at the outset.

In considering the **human factor,** Allen points out that conditions are rarely ideal, that human nature is imperfect, and that the treatment of diabetes is long and onerous for both physician and patient. He believes that the idea that diabetes is merely the weakness of a bodily function, and not necessarily a progressive, fatal disease, might lessen the bewilderment and feeling of helplessness concerning diabetes, which now, too often, prevails among physicians.

It is his idea also that the fear of suddenly withdrawing carbohydrate from the diet, especially on account of ketonuria, should be strongly combated, since the starvation method of testing tolerance described will stop glycosuria promptly, and, instead of producing ketonuria, will abolish it if it already exists. Both glycosuria and marked ketonuria can apparently be stopped in every diabetic patient within a very few days.

As a matter of fact, experience with the starvation method has not proved to be as serious a hardship to patients as might have been surmised. Though the treatment is rigorous, in the severe cases, the patients admit that they feel more comfortable, and soon prefer to endure the low diet rather than to return to their sufferings on a more abundant diet.

When a patient has been thoroughly studied, his tolerance tested, and his régime outlined, he is given the following **instructions:**

1. Collect the whole 24 hour urine daily and test a portion of it by Benedict's method for sugar.
2. Should sugar appear in the urine, fast immediately for one day, and reduce the diet a little more.
3. Stay in bed and fast completely at stated intervals (say for one day every second or fourth week), even if no sugar appears in the urine.
4. Live on a diet containing certain articles of food in certain approximate quantities.
5. Instead of weighing the food, the patient is to weigh himself at least once a week, and is never to allow his weight to rise above a stated figure. This figure is placed below the original maximal weight, and is made lower in proportion to the severity of the diabetes present.

For convenience, Dr. E. P. Joslin of Boston has prepared a small filing card (See next two pages) for tolerance testing in diabetes. These cards may be obtained from Thomas Groom & Co., Inc., 105 State Street, Boston:

**Fasting.**—Fast until sugar-free. Drink water freely and tea, coffee and clear meat broth as desired. In very severe, long standing and complicated cases, without otherwise changing habits or diet, omit fat, after two days omit protein and halve carbohydrate daily to 10 grams, then fast.

**Carbohydrate Tolerance.**—When the 24 hour urine is sugar-free, add 150 grams of 5 per cent vegetables, and continue to add 5 grams carbohydrates daily up to 20 and then 5 grams every other day, passing successively upward through the 5, 10 and 15 per cent vegetables, 5 and 10 per cent fruits, potato and oatmeal to bread, unless sugar appears or the tolerance reaches 3 grams carbohydrate per kilogram body weight.

**Protein Tolerance.**—When the urine has been sugar-free for 2 days, add 20 grams protein (3 eggs) and thereafter 15 grams protein daily in the form of meat until the patient is receiving 1 gram protein per kilogram body weight, or if the carbohydrate tolerance is zero, only ¾ gram per kilogram body weight.

**Fat Tolerance.**—While testing the protein tolerance, a small quantity of fat is included in the eggs and meat given. Add no more fat until the protein reaches 1 gram per kilogram (unless the protein tolerance is below this figure) but then add 25 grams daily until the patient ceases to lose weight or receives not over 40 calories per kilogram body weight.

**Reappearance of Sugar.**—The return of sugar demands fasting for 24 hours or until sugar-free. The diet is then increased twice as rapidly as before, but the carbohydrate should not exceed half the former tolerance until the urine has been sugar-free for 2 weeks, and it should not then be increased more than 5 grams per week.

**Weekly Fast Days.**—Whenever the tolerance is less than 20 grams carbohydrate, fasting should be practised one day in seven; when the tolerance is between 20 and 50 grams carbohydrate, upon the weekly fast day 5 per cent vegetables and one-half the usual quantity of protein and fat are allowed; when the tolerance is between 50 and 100 grams carbohydrate, the 10 and 15 per cent vegetables are added as well. If the tolerance is more than 100 grams carbohydrate, upon weekly fast days the carbohydrate should be halved.

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| | | | | |
|---|---|---|---|---|
| 1 | gram | protein, | 4 | calories. |
| 1 | " | carbohydrate, | 4 | " |
| 1 | " | fat, | 9 | " |
| 1 | " | alcohol, | 7 | " |
| 6.25 | " | protein contain 1 g. nitrogen. | | |

1 kilogram = 2.2 pounds.
30 grams (g) or cubic centimeters (c.c.) = 1 ounce.
A patient "at rest" requires 25 to 30 calories per kilogram body weight.

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Consult Chemical Composition American Food Materials, Bull. 28, U. S. Dept. Agriculture, by sending 10 cents in coin to Supt. of Documents, Washington, D. C., also Annual Report Conn. Agricultural Experiment Station, New Haven, Conn., Food Products and Drugs, 1913, Part 1, Section 1.—Free.

**STRICT DIET. Meats, Fish, Broths, Gelatine, Eggs, Butter, Olive Oil, Coffee, Tea and Cracked Cocoa.**

FOODS ARRANGED APPROXIMATELY ACCORDING TO % OF CARBOHYDRATES.

| | 5% * | 10% | 15% | 20% |
|---|---|---|---|---|
| VEGETABLES | Lettuce, Spinach, Sauerkraut, String Beans, Celery, Asparagus, Cucumbers, Brussels Sprouts, Sorrel, Endive, Dandelion Greens, Swiss Chard, Sea Kale, Cauliflower, Tomatoes, Rhubarb, Egg Plant, Leeks, Beet Greens, Water Cress, Cabbage, Radishes, Pumpkin, Kohlrabi, Broccoli, Vegetable Marrow | Onions, Squash, Turnip, Carrots, Okra, Mushrooms, Beets | Green Peas, Artichokes, Parsnips, Canned Lima Beans | Potatoes, Shell Beans, Baked Beans, Green Corn, Boiled Rice, Boiled Macaroni |
| FRUITS | Ripe Olives (20% fat), Grape Fruit | Lemons, Oranges, Cranberries, Strawberries, Blackberries, Gooseberries, Peaches, Pineapple, Watermelon | Apples, Pears, Apricots, Blueberries, Cherries, Currants, Raspberries, Huckleberries | Plums, Bananas |
| NUTS | Butternuts, Pignolias | Brazil Nuts, Black Walnuts, Hickory Nuts, Pecans, Filberts | Almonds, Walnuts (Eng.), Beechnuts, Pistachios, Pine Nuts | Peanuts; 40%: Chestnuts |
| MISC. | Unsweetened Pickle, Clams, Oysters, Scallops, Liver, Fish Roe | | | |

* Reckon available carbohydrates in vegetables of 5% group as 3%, of 10% group as 6%.

| (30 grams; 1 oz.) CONTAIN APPROXIMATELY | PROTEIN G. | FAT G. | CARBOHYDRATES G. | CALORIES |
|---|---|---|---|---|
| Oatmeal, dry wgt | 5 | 2 | 20 | 110 |
| Meat (uncooked, lean) | 6 | 2 | 0 | 40 |
| " (cooked, lean) | 8 | 3 | 0 | 60 |
| Broth | 0.7 | 0 | 0 | 3 |
| Potato | 1 | 0 | 6 | 25 |
| Bacon | 5 | 15 | 0 | 155 |
| Cream, 40% | 1 | 12 | 1 | 120 |
| " 20% | 1 | 6 | 1 | 60 |
| Milk | 1 | 1 | 2 | 20 |
| Bread | 3 | 0 | 18 | 90 |
| Butter | 0 | 25 | 0 | 240 |
| Egg (one) | 6 | 5 | 0 | 75 |
| Brazil Nuts | 5 | 20 | 2 | 210 |
| Orange or Grape Fruit (one) | 0 | 0 | 10 | 40 |
| Vegetables 5 and 10% group | .05 | 0 | 1 or 2 | 6 or 10 |

Form J 8. THOMAS GROOM & Co., INC., 105 State St., Boston.

The menus in Hill and Eckman's "Starvation-Treatment of Diabetes" will be found convenient in arranging the diet of diabetic patients during and after the testing of the carbohydrate tolerance.

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# F. Gout

## 1. Introduction

### (a) *Conception of the Malady*

Gout is a disturbance of the metabolism of purins, often hereditary, in which an excess of uric acid accumulates in the blood and in the tissues. In the *typical cases* ("regular" gout), it leads to recurring attacks of acute and extremely painful arthritis (*arthritis urica acuta*) especially in the joints of the lower extremities, or to deposits of urates in cartilage, bone or connective tissue (so-called *tophi*), or to both; in *atypical cases*, it may manifest itself clinically in other ways ("irregular" gout). In both typical and atypical cases, the symptoms are aggravated by alcoholism and by a purin-rich diet, and may be ameliorated by the administration of aspirin or of colchicum; the accumulation of uric acid in the body can be lessened by a purin-free diet, by active physical exercise, and by atophan-therapy.

### (b) *History*

History.—The disease was known to Hippocrates, the attacks in the feet being called *podagra*—hence the later names, *gonagra, ischiagra, chiragra, omagra, rachisagra*, for involvement of other parts. Galen connected gout with "high living" and gave the name *tophi* to the "gouty deposits." Actius knew that gout could be inherited. Sydenham, suffering from gout himself, gave an admirable clinical description of the disease.

Uric acid was found in tophi in 1797 (Wollaston), and in the blood of gouty patients in 1847 (Garrod). The relation of uric acid to the purins was thoroughly established by Emil Fischer, and soon the conception of gout as a disturbance of the metabolism of purins and their forerunners (the nucleins) arose, the distinction between the uric acid derived from the nucleins and purins of the food (*exogenous*) and the uric acid arising from the catabolism of the nuclei of the body cells (*endogenous*) being set up by Burian and Schur, and by Siven. Brugsch and Schittenhelm showed that while uric acid ceases to be demonstrable by a given method in the blood of normal persons on a purin-free diet, this is not the case in the gouty. The physiology of nuclein metabolism has been carefully studied by Kossel and his pupils and, especially in its enzymatic relations, by Walter Jones and his pupils, and by Levene and his associates.

Miller and Jones have found that the distribution of the ferments that attack nucleic acid and the purins does not differ in the organs of a person dead of gout from the distribution in persons free from gout.

The origin of the colchicum therapy is obscure. In 2-phenylchinolin-4-carbonic acid (atophan) we possess a drug that leads to marked increase in the excretion of uric acid through the kidneys (Nicolaier and Dohrn; Weintraud).

## 2. Clinical Studies of Gout

### (*a*) *Etiology*

*Heredity* is an important factor, demonstrable in over half the cases in consultation practice, though less obvious in patients in the public wards of hospitals. *Alcohol* is an exciting cause, heavy beers, ale, porter, champagne and port wine being apparently more pernicious than whisky and the lighter wines and beers, though alcohol in any form is injurious in the predisposed. True gout, however, may occur in total abstainers. *Plethoric persons* are more often affected than those of asthenic habitus. *High living*, especially overindulgence in meats and other purin-rich foods, may lead to gout, especially in people who follow a *sedentary life,* and do not take physical exercise regularly. Long-continued *lead poisoning* is a not uncommon cause.

Though true gout may occur in the thin and abstemious, it should be remembered that the so-called "poor man's gout" or *arthritis pauperum* of the older writers is a different disease, namely, "primary" chronic progressive polyarthritis, and is not due to a disturbance in the metabolism of purins (See Part XI).

### (*b*) *Clinical Forms of Gout*

We distinguish several forms including (1) typical acute gouty arthritic attacks, (2) an acute or subacute polyarticular form of gout, (3) renal gout, (4) more irregular forms of gout including (a) chronic gouty arthritis and (b) abarticular gout.

#### i. The Typical Acute Attack of Arthritic Gout

(*Arthritis urica acuta*)

The *onset* is sudden, usually in the night, the patient being awakened in the early morning hours by excruciating pain in the joint, most often the metatarsophalangeal joint of the left *great toe.* The *pain* increases in severity, becoming almost unbearable. Next morning, the *joint* is found to be swollen, and, during the day, the swelling increases, and the surface of the joint becomes hot and red. The *attack* lasts several days, with nocturnal exacerbations of the pain; then the symptoms subside, the skin over the joint sometimes desquamates and the joint remains tender for some time. Though usually *monarticular,* other joints (ankle, knee, wrist, elbow), may become similarly involved in two or three days after onset.

There is often *fever,* with *anorexia, weakness* and marked mental *irritability* or *depression.*

The *first attack* rarely comes before the thirtieth year of life; most often it is in the early forties, in contrast with acute rheumatic fever that is rare after thirty or forty. Occasionally, a first attack of gout is deferred until late in life (seventieth year, eightieth year). When the uric-acid curve in the urine is followed, it is found to show a characteristic type (*vide infra*). Once such a typical attack has occurred, it is likely to be followed by *later attacks* once or twice a year, especially in the spring and autumn, after indiscretions in diet, work, or sexual indulgence. In many instances, attacks can be prevented altogether, provided, after a correct diagnosis has been made, the patient has the will-power to follow a rigid regime. In at least one-third of the cases, deposits of mononatrium urate—the so-called *tophi*—sooner or later appear, most often in the ear, and, occasionally,

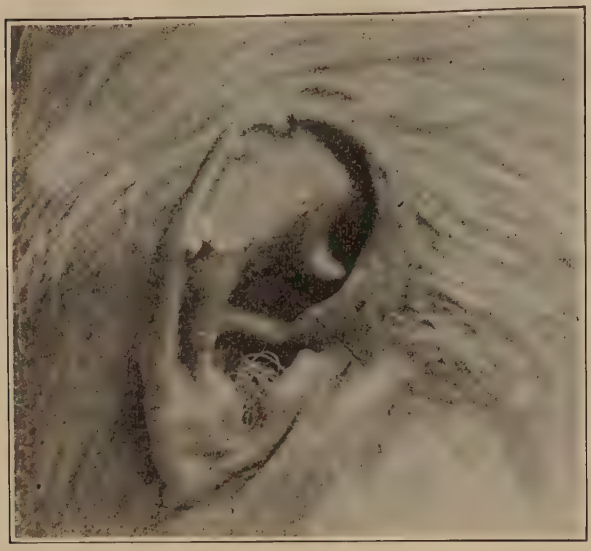

Fig. 641.—Tophi in Right Ear. Gout, in Chronic Nephropathy. (Med. Service, J. H. H.; Photograph by Dr. Brotherhood.)

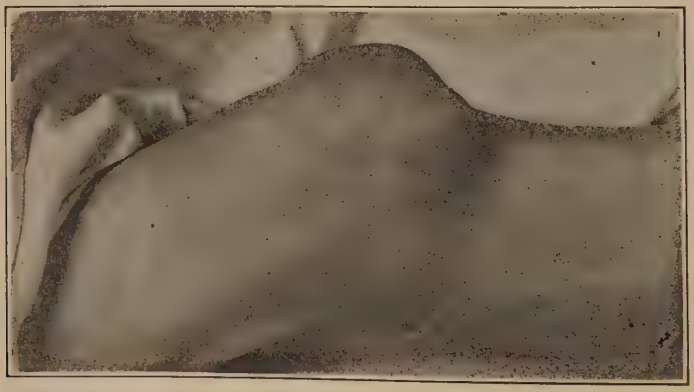

Fig. 642.—Tophi About the Knee-joint; from the Same Case as Fig. 641. (Med. Service, J. H. H.; Photograph by Dr. Brotherhood.)

beneath the skin elsewhere (finger-tip, alae nasi, eyelid, palm, etc). Larger tophi may appear in the connective tissue, usually near a

joint (feet, hands), or on tendons or tendon-sheaths; not infrequently they occur as incrustations of bursae (particularly over the olecranon and in front of the patella), and occasionally they are met with in the muscles (M. trapezius) or in the mucous membranes. Similar deposits may occur in the bones themselves, especially in the ends of bones near affected joints; such deposits are followed by absorption of the lime salts in localized areas and yield characteristic pictures in x-ray plates (clear spherical areas, often surrounded by a dark margin). They are of great diagnostic value as they lie in the bones themselves, not in enchondroses or exostoses as do the cysts seen in other chronic arthropathies. If a tophus be needled, particles can be obtained for microscopic examination. The crystals are characteristic; they yield the murexid reaction.

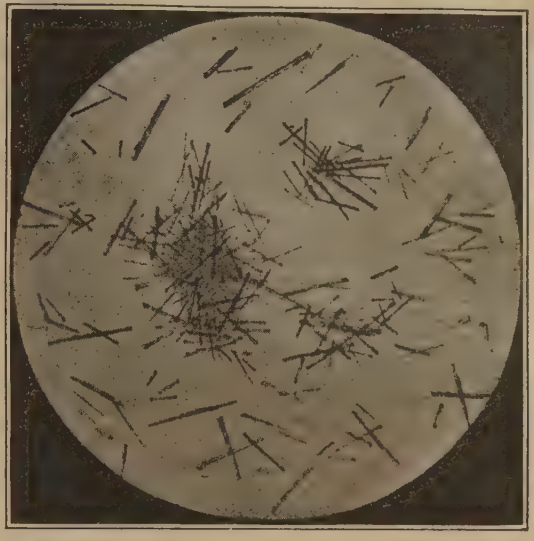

Fig. 643.—Sodium Biurate Crystals from a Tophus in Gout. (After H. Sahli, "Lehrb. d. klin. Untersuch.," published by F. Deuticke, Leipzig.)

This typical gout is usually a true metabolic gout, in which the whole metabolism of nucleins and purins is disturbed; there is slowing of uric-acid formation and delay of uric-acid excretion.

### ii. The Polyarticular Form of Gout

(*Polyarthritis urica acuta seu subacuta*)

First described by Lecorché, this rarer form of gout has gradually attained to general recognition. It is characterized by involvement of many joints with fever, the attacks lasting longer than the typical acute gouty attacks, so that the true nature may be easily overlooked, and an infectious arthritis be suspected. The large joints (ankle, knee, shoulder) are often involved, with swelling of the joint capsules and effusion into the joints. According to Brugsch, the output of endogenous uric acid in the urine is exceedingly high (0.5-0.6 g.) in these cases, and at the same time the uric-acid content of the blood serum is also exceedingly high (10-12 mg. mononatrium urate in 100 c.c.); he therefore suggests that in this form of gout, we have to deal with (1) a *hyperuricemia* and (2) a so-called *uric-acid diabetes.*

The gout that occurs in leukemia shows similar conditions in the blood and urine; in **leukemic gout**, there is an *over-production* of uric acid owing to the disintegration of the nucleins of the leukocytes, not unlike the over-production following upon the crisis in pneumonia.

### iii. Renal Gout

In this disease, the symptoms of genuine contracted kidney (with heart hypertrophy and arterial hypertension) stand in the foreground. In some cases, lead is the etiological agent. The kidneys fail to excrete uric acid normally, and a "retention uricemia" results, so that the endogenous-uric-acid output in the urine is low, the uric-acid content of the blood serum high. The patient may suffer from acute gouty attacks; more often, there is slow development of tophi and of a chronic deforming arthritis. This "renal gout" is not to be confused with the late changes often occurring in the kidneys in long-standing "metabolic gout." The post mortem statistics of English observers (Ord, Greenfield, Norman Moore, Luff) in renal gout are very striking.

### iv. "Irregular" Forms of Gout

Of these, two forms have been differentiated: (1) chronic gouty arthritis, and (2) abarticular gout.

#### 1. *Chronic Gouty Arthritis* (*Arthritis urica chronica*)

This may follow upon acute gouty arthritis, but typical acute attacks are often missing in the anamnesis. In such cases, there may be difficulty in differentiating the disease from other chronic arthropathies, though, in the majority of cases, a search for tophi, and x-ray examinations, will furnish the necessary diagnostic criteria. In the absence of tophi and of typical gouty lesions in x-ray plates, the diagnosis can be helped out by determinations of the content of the blood serum in endogenous uric acid, and by tests for the rapidity of excretion of exogenous purins in the urine.

Interest in the relation of gout to hypertrophic osteo-arthritis (arthritis deformans of the German writers) is increasing. I was much struck by specimens recently shown me by Dr. Strangeways of the Cambridge Research Hospital, in which urate deposits were clearly present in joints showing hypertrophic osteo-arthritic lesions. It is conceivable that even degrees of uricemia insufficient to cause crystalline deposits in the joints may suffice to initiate the degenerative and hyperplastic lesions of "hypertrophic osteo-arthritis." Careful studies of the purin metabolism are, accordingly, urgently indicated in this group of cases.

### 2. *Abarticular Gout*

Patients with faulty metabolism of purins may, with or without arthritic attacks, suffer from other symptoms. Thus in the "gouty diathesis," it is not uncommon to meet with paroxysmal *disturbances of digestion* (gastric, intestinal), *iritis, episcleritis, pharyngitis, parotitis, eczemas, cyclothymic depression, neuralgias, neuritis, cardiac arhythmias, phlebitis,* or *bronchitis.* Great care should, however, be exercised before attributing such conditions to faulty purin metabolism; in doubtful cases, other possible causes should be thoroughly canvassed, and before arriving at a positive conclusion, the support of actual anomalies in the metabolism of purins, based upon quantitative tests by modern methods, should be required. At many of the spas, the diagnosis of gout is made in an almost frivolous manner!

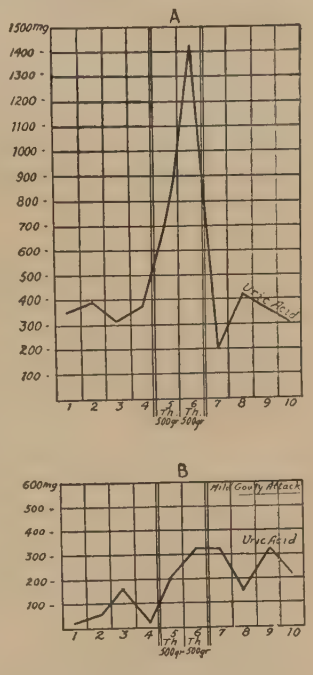


Fig. 644.—A, Uric-Acid Output Following Ingestion of Thymus Gland in Normal Person. B, Uric-Acid Output Following Ingestion of Thymus Gland in Gouty Person. (After F. Umber, "Lehrb. d. Ernährung u. d. Stoffwechselkrankh.," published by Urban & Schwarzenberg, Berlin.)

## (c) *Investigations of the Metabolism of Purins in Gout*

### i. Introduction

Since Kossel showed that uric acid can come from the purin bases, and since Emil Fischer cleared up the relationships of the various purin bodies to one another, the metabolic study of gout has become intensely interesting.

The origin of the uric acid of the blood and of the urine, the differences between plant nucleic acid and animal nucleic acid, the ferments concerned in the metabolism of nucleins and purins, have already been thoroughly discussed (See Part XIII, Sec. i).

About 50 per cent of the purin bases taken in as nucleo-proteids and other purin-containing substances in the food (*exogenous purins*) are, normally, eliminated within 48 hours in the urine as uric acid (*exogenous uric acid of the urine*). The other half is rather difficult to account for. As far as we know, the human body does not possess the power of oxidizing uric acid, since the ferment, uricase, which changes uric acid to allantoin in many animals, is absent from human beings.

The uric acid of the urine derived from the metabolism of the nucleic acid of the nuclei of the body itself, from extranuclear mononucleotides, and from the hypoxanthin of the muscles is known as the *"endogenous uric*

*acid of the urine"*; it varies in amount for each person but is almost constant for the same person, even at intervals of several years. Thus, if a healthy man be placed upon a purin-free diet (*q. v.*) for several days, the uric-acid content of his urine will soon assume a constant value, the amount in each 24 hours varying, according to the person, between 0.3 and 0.6 g. (in females between 0.3 and 0.5 g.). Once this endogenous-uric-acid value for the urine of a given person has been determined, the study of his exogenous purin metabolism becomes possible. One has only to add a known amount of purin-containing food, preferably the sodium salt of one of the nucleic acids, to the otherwise purin-free diet. and to follow the excretion of exogenous purins in the urine, *i. e.*, the uric acid in the urine in excess of the constant "endogenous-uric-acid value." Here, two things are important: (1) the *absolute amount* of exogenous purin eliminated in the urine (normally 50 per cent of the purin intake) and (2) the *time* taken to eliminate it (normally 24 to 48 hours).

### ii. The Endogenous-uric-acid Content of the Urine in Gout

In periods between attacks, the endogenous output is constant for each person, though it varies in different gouty patients. Brugsch and Schittenhelm have classified endogenous outputs as follows:

1. 0.0-0.3 g. = abnormally low.
2. 0.3-0.4 g. = lower limit of normal.
3. 0.4-0.6 g. = upper limit of normal.
4. 0.6 or more = abnormally high.

In gouty patients, they found the endogenous output (1) abnormally low in 43 per cent of the cases, (2) at the lower limit of normal in 36 per cent, (3) at the upper limit of normal in 21 per cent and (4) abnormally high in none of the cases. For the behavior of the endogenous output just before, during, and just after a gouty attack (*vide infra*).

### iii. The Exogenous-uric-acid Content of the Urine in Gout and the Time Taken to Excrete Uric Acid of Exogenous Origin

Exact studies have shown that the important deviation from the normal in gout, as regards the metabolism of exogenous purins, is the *delay* in the excretion. If a definite amount of purins be added to a purin-free diet, the resulting exogenous uric acid of the urine instead of being excreted in 24 to 48 hours as normally, requires four, five or

more days for its elimination; and, in the end, the absolute amount excreted is less than normal (*i. e.,* less than 50 per cent of the purin intake).[1] As yet we do not know how uric acid is destroyed in the human body, if indeed it can be destroyed at all. We are much better informed about the destruction of uric acid in animals, since in them the uricolytic ferment, uricase, is active. Why is the exogenous purin metabolism so delayed in gout? We do not certainly know. It might depend upon imperfect action of the ferments, either of those of the intestine that split the nucleic acids and prepare them for absorption, or of those of the intestinal wall and of the liver that convert one purin into another; the possibility of delay in mobilization from the hepatic depot (vegetative nervous system?) must also be kept in mind, and the possibility of slowed passage of uric acid through the renal filter must not be lost sight of. *The single fact at present available is the demonstration by Miller and Jones of a normal distribution of the ferments in the organs of the gouty.*

### iv. The Uric-acid Content of the Blood in Gout

In 1848, Garrod devised his "thread test" to demonstrate the presence of uric acid in the blood serum in gout. By more delicate chemical methods, introduced later, it has been shown that uric acid is always present in the blood of the gouty patient, even on a purin-free diet; indeed, this constant "endogenous uricemia" is of real diagnostic value in gout, and it is a pity that the methods as yet devised for demonstrating it are so difficult. Every effort should be made to work out a simpler method that is reliable. Fortunately, the colorimetric method of Folin and Denis is now available; since it is comparatively easy of application there may be hope that before long we may have many more accurate studies of uric-acid metabolism in human beings than were formerly possible.

In healthy persons, the content of the blood in endogenous uric acid (after three days of purin-free diet) does not exceed 1-1.5 or, at most, 2 mg. in 100 c.c.; in the gouty, values varying between 6 and 10 mg. of mononatrium urate are found; indeed, in a gouty attack, or just before one, the endogenous values may be as high as 10-12 mg. of mononatrium urate (Brugsch), the content then exceeding that of the blood in the intervals between attacks. In gout associated with contracted kidneys

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[1] Since the amounts of urea and ammonia excreted are increased, it has been suggested that this diminution in the absolute amount of uric acid excreted depends either on increased destruction of uric acid (owing to the prolongation of the whole process) or to a displacement (in the liver?) of other forerunners of urea and $NH_3$ with retention of purin bases (Brugsch).

the content may be very high (10-20 mg.) even in the intervals between attacks.[1]

The endogenous uric acid in the blood in gout has recently been studied by R. A. Kocher and also by J. H. Pratt by means of the colorimetric method of Folin and Denis. Kocher found on the average in 17 gouty patients 4.64 mg. per 100 g. blood; the highest amount found was 7.2 mg., the lowest amount 1.61 mg. Pratt found amounts varying between 3.1 and 5.5 mg.; after atophan, the amount fell to normal.

It is probable that the uric acid in the blood may exist in more than one form. The matter is not yet settled, but two hypotheses have been formed regarding it.

According to one, that of Gudzent, uric acid forms *two series of primary salts,* distinguishable by their solubility. The first series (*a-salts* or *lactim-urates*) are unstable and are quickly changed into the more stable second series (*b-salts* or *lactim-urates*). If the uric acid in the blood exists in the lactim-form, then, in gout, the blood is approximately a saturated solution of lactim-urate on a purin-free diet, so that, on a purin-containing diet, it becomes supersaturated.

According to a second view, that of Bechold and Ziegler, uric acid may exist in the blood in *colloidal sclution,* and some believe that such a colloidal phase may be responsible for the differences between the blood in gout and in normal states. The topic is being actively investigated, and, ere long, we shall be better informed concerning it.

Why does uric acid accumulate in the blood in gout? This is a vexed question, to which no wholly satisfactory answer can, as yet, be made. The older view that in gout we have always to do with a retention-uricemia due to an anatomical, or to at least a functional, change in the kidneys has, of late, been challenged. Since most gouty patients are able, especially at times of acute attacks, to excrete large quantities of uric acid in the urine; since the endogenous uricemia in gout has a constant, relatively low value in contrast with the variable value (sometimes high, sometimes low) met with in severe nephropathies; since purin bases fed to gouty patients who have no signs of renal disease are excreted either as exogenous uric acid or as urea in the urine; and since, in exogenous-uric-acid formation in gouty patients with healthy kidneys, there is no real stasis of uric acid behind the kidneys, for, though the uric-acid content of the blood is higher than normal for a little longer period than in the non-gouty, the normal amount is ultimately excreted—it is maintained that, in true "metabolic gout," as contrasted and with "renal gout," the primary cause of the accumulation of uric acid in the blood does not lie in the kidneys (Brugsch and Schittenhelm).

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[1] It should be kept in mind that, in the absence of true metabolic gout, a high value for endogenous uricemia may be met with in chronic nephropathies (*retention-uricemia*), in leukemia, and after the crisis in pneumonia (*disintegrating leukocytes*), and, temporarily, after exposure of the skin to x-rays.

Two other hypotheses have been raised to explain the accumulation in true metabolic gout: (1) that destruction of uric acid (uricolysis) is less than normal, a hypothesis that has as yet no basis, since we know nothing of uricolysis in human beings, uricase being absent from human organs, and (2) that a certain relation exists between the rate at which the liver works (in purin metabolism) and the rate at which the kidney excretes uric acid, in other words, that when the metabolic changes in the purins in the liver (and intestine?) are disturbed, the threshold for uric-acid excretion by the kidneys is reflexly altered. According to this latter hypothesis the primary change in "true metabolic gout" is in uric-acid formation, the secondary change in the increased threshold for uric-acid excretion by the kidneys; and with these changes are contrasted the changes in "renal gout," in which the primary change is in the kidneys, and it is responsible for a secondary uricemia (by retention).

### v. The Uric-acid Excretion in the Acute Gouty Attack

Whether on a purin-free diet, or on a mixed diet with constant purin content, the gouty patient just before, during, and after an acute attack excretes urine that is peculiar and characteristic. If the quantities of uric acid excreted each day be determined and charted, the curve is divisible into three stages: (1) a stage in which the amounts excreted

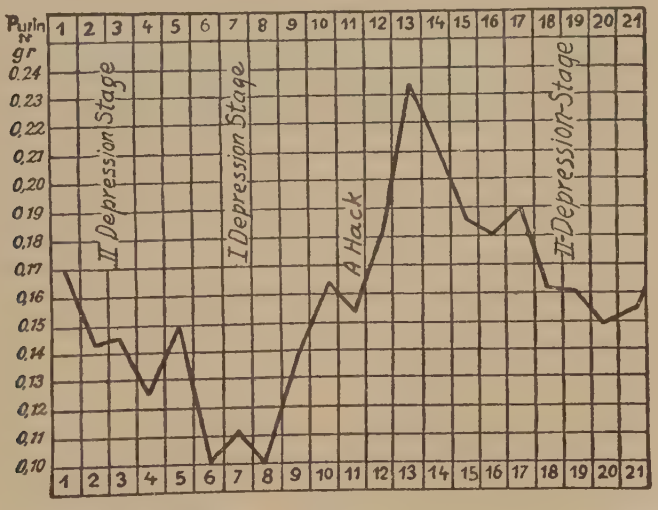


Fig. 645.—Curve of Uric-acid Output in Gout. The Output Is Always Low Between Attacks, Sinking Markedly Just Before an Attack. During the Attack, the Output Is Greatly Increased, Falling Again in a Few Days. (After F. Umber, "Lehrb. d. Ernährung u. d. Stoffwechselkrankh.," published by Urban & Schwarzenberg, Berlin.)

are small (*anacritical stage of depression*), this stage lasting from one to four days; (2) a stage in which excessive amounts are excreted (*stage of increased excretion*), this stage beginning with the onset of the attack

and reaching its acme on the first, second, or, occasionally, on the third day; and (3) a stage in which the amounts excreted are again small, even smaller than the normal endogenous output of the person (*post-critical stage of depression*). In stages (1) and (2), the uric-acid content of the blood is increased. If the total N (intake and output) be followed in an attack, positive N-balances are usually found in stages (1) and (3). A study of the feces at the time of an acute attack reveals an excessive N-output in the stools (as much as 8 per cent of the intake).

The *total metabolism* (calories) in gout seems to undergo no change, either in attacks, or *between* them.

### vi. The Effect of Atophan upon Purin Excretion

*Atophan,* 2-phenylchinolin-4-carbonic acid and the chemically closely allied (but tasteless) *isatophan,* when given in 0.5 g. doses four to six times a day, for a couple of days, will lead to a marked increase in the output of uric acid in the urine. This is true in gouty as well as in healthy persons, and it holds when they are on a purin-free diet (endogenous uric acid) or on a purin-containing diet (exogenous uric acid), the only exception being cases of "renal gout."

The mode of action of atophan is now being studied. Some think that it acts directly on the kidneys, causing an elective increase in uric-acid excretion; others look upon the renal excretion as secondary, and think that the primary effect of atophan is to "mobilize" uric acid from a reserve depot (liver?), much as epinephrin is supposed to "mobilize" glucose from the glycogen-containing liver. To obtain the optimal effect in gout, it is given between attacks, every two weeks, for two days at a time. If an attack be threatened, it may sometimes be aborted by the immediate administration of atophan (in the "anacritical depression stage"). Atophan should not be given during an actual attack, for, as we have seen, at such times the kidneys are already excreting an excess of uric acid. In the polyarticular form of gout (with marked hyperuricemia), atophan may with advantage be given continuously (1-2 g. daily), rather than intermittently as in ordinary gout.

## (*d*) *The Diagnosis of Gout*

The main points have been referred to under the symptoms. The disease is much more common in America than is generally supposed, and many cases go unrecognized. When typical attacks, tophi, or characteristic x-ray changes, are lacking, the recognition may be very difficult, since it then depends upon the making of metabolic tests that require exact chemical analyses. Of such metabolic tests, the demonstration of (1) endogenous uricemia and of (2) delayed excretion of exogenous purins are the most important. *Examinations of the uric-acid*

*content of the urine, in the absence of rigid dietetic control (with known purin intake) are, of course, worthless.* It is distressing to think of the

Fig. 646.—Röntgenogram of the Hand in Gout. (After F. Umber, "Lehrb. d. Ernährung u. d. Stoffwechselkrankh.," published by Urban & Schwarzenberg, Berlin.)

waste of time and money, and of the clinical illusions, to which such examinations have given rise, and alas, continue to give rise!

### (e) *The Purin Content of Foodstuffs*

The percentage of purins in common foodstuffs has already been given in a table. The following lists may, in addition, be helpful to the practitioner in dealing with cases of gout.

A. *Purin-free foods, containing no purins or only traces.*
Bread, cereals (oatmeal, rice, sago, tapioca, etc.); fruits (bananas, pineapples, peaches, grapes, pears, plums, cranberries, oranges, apricots, huckleberries, apples); nuts (walnuts, hazelnuts, almonds); certain vegetables (cucumbers, cabbage, turnips, onions, tomatoes); milk, cream, butter, certain cheeses (Edam, Swiss, Gervais, Roquefort); eggs.

B. *Purin-poor foods, containing only small amounts.*
Certain cheeses (cream cheese; ordinary American cheese); caviar; certain vegetables (lettuce, radishes, cauliflower, celery, asparagus, string beans, potatoes, carrots).

C. *Purin-containing foods.*
Meats (beef, veal, mutton, pork, tongue, brain, chicken, goose, venison, fish, oysters, crabs, lobsters); certain vegetables (spinach, kohlrabi, peas, beans).

D. *Foods extremely rich in purins.*
Sweetbreads, liver, kidney, herring, sardines, anchovies. Bouillon is rich in purins; beer contains considerable nucleic acid from yeast; coffee, tea, chocolate and cocoa contain methylpurins, but they do not give rise to uric acid. For the exact content of the various foodstuffs in purins, consult the table already given (See Part XIII, Sec. i).

When making tests requiring a purin-free diet, a sample diet has already been given (see Determinations of Purin Metabolism). In addition, the following meals may be found convenient:

*Breakfast:* Coffee (decaffeinized) with cream, toast, butter, marmalade, eggs, milk.

*Dinner:* Vegetable or cream soup (no meat or meat extract), potato, vegetable from list A with butter; stewed fruit, rice, sago, or tapioca pudding.

*Supper:* Omelette, or scrambled eggs, cheese, bread and butter, fruit, milk (hot or cold).

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# Part XIV

# Diagnosis of Diseases of the Glands of Internal Secretion (The Endocrinopathies)

## A. Introduction

The "physiological law" of Treviranus asserted that the excreta of one organ are necessary foodstuffs of other organs. Modern studies have shown us that certain organs—so-called **glands of internal secretion,** or **endocrine glands**—produce substances that are of extreme importance for the function of other organs distant from them. Since these substances are carried from the gland that produces them through the blood to the organs that they affect, they have been called by Starling **"chemical messengers"** or **"hormones."**

Clinicians, applying these physiological studies, have come to recognize definite syndromes that appear to be due to **hyperfunction, hypofunction** and **dysfunction** of these glands. These syndromes, while usually easily recognizable, exhibit manifold variations, owing to three complicating facts: (1) the hormones act on organs partly through the vegetative or autonomic nervous systems that innervate them, partly directly upon the cells of the organs themselves, (2) an over-function, or an under-function, of one endocrine gland leads, sooner or later, to disturbances of function in other endocrine glands, for these glands, taken together, form a united system—the so-called *"hormonopoietic system"* (Falta), and (3) the original make-up of the organs is unique for each human being. In the sense of Treviranus, every tissue of the body would be included among the makers of internal secretions, but it is customary to restrict the system to a special group of glands, viz:—(1) the *thyroid gland,* (2) the *hypophysis cerebri* or *pituitary body,* (3) the *chromaffin tissues,* including the medulla of the suprarenals, (4) the *interrenal system,* represented in man by the cortex of the suprarenals, (5) the *para-*

*thyroid glands,* (6) the *genital glands* or *gonads* (testes and ovaries), (7) the *thymus gland,* (8) the *epiphysis cerebri* or *pineal gland,* and (9) certain portions of the *pancreas.*

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# B. Diseases of the Thyroid Gland

(*The Thyropathies*)

Conceptions of the internal secretions and their disturbances have grown largely out of studies of the thyroid gland and its functions; for this reason we can scarcely do better than to begin the study of anomalies of internal secretion with a consideration of the thyropathies.

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## 1. Normal Functions of the Thyroid Gland

### (*a*) *Relations of the Thyroid to Iodin Metabolism*

The thyroid gland seems to be the central organ for iodin metabolism. The iodin of the food is normally converted in this gland into an organic substance, called *iodothyroglobulin,* a body from which, on treatment with acids, a chemical substance, very rich in iodin, the so-called *iodothyrin,* can be split off. The *colloid* of the follicles of the thyroid contains the specific iodin-containing secretion, and this is, normally, given off into the blood (probably by way of the lymph channels of the gland) as required for the functions of the rest of the body.

This organic compound of iodin of the thyroid secretion is a "masked iodin," that is to say, it differs in action from inorganic iodin, perhaps because it enters into function in places in the body not entirely identical with those accessible to inorganic iodin or for other reasons still to be discovered.

Normally, the body appears to maintain an "iodin equilibrium." If an excess of iodin be taken in, the surplus is, within limits, promptly

excreted. In abnormal states, the iodin equilibrium may be disturbed, with iodin deficit on the one hand, or iodin retention on the other. Iodin retention seems to be favored by the administration of phosphates.

Many believe that iodothyroglobulin possesses all the properties of desiccated thyroid gland, and assume that the functions of the thyroid are limited to the production and distribution of this iodothyroglobulin. Others, while admitting the central position of the iodin body, maintain that a whole series of other substances are produced by the gland, and that a full understanding of the functions of the thyroid must await their recognition and an examination of their physiological actions.

The iodin compound, once in the blood, appears to have an especial affinity for certain tissues, particularly for (1) the neurons of the vegetative nervous systems, and (2) the cells concerned in combustion processes (oxidations); in addition, it seems to influence profoundly, either directly or indirectly, the cerebrum (psychic processes), the muscles (voluntary, cardiac), the lymphocytogenous organs (thymus, lymphatic glands), and the other glands of internal secretion.

### (*b*) *Relations of the Thyroid to the Autonomic Nervous System*

Both *vegetative nervous systems* (the sympathetic and the autonomic proper) are stimulated by the internal secretion of the thyroid gland. The tonus of the two systems is closely related to the thyroid function. The relations are strikingly illustrated in abnormal cases (See *hyperthyroidism* and *myxedema*).

### (*c*) *Relations of the Thyroid to the Processes of Metabolism*

The *combustion processes of the body* appear to be in part regulated by the thyroid secretion, which acts like a "fan to the fire"; when the secretion is excessive, the total metabolism (calories) is increased, as seen in the emaciation of Graves' disease; when the secretion is defective, as in beginning myxedema, the total combustion is diminished, and obesity easily develops. The *protein metabolism* is also specifically affected by the thyroid secretion (See cachexias). The *mineral metabolism* is also markedly influenced (See below).

### (*d*) *Variations in the Functions of the Thyroid*

Indeed, all the functions of the thyroid are most easily studied in pathological cases in which we believe there is an over-function or an under-function of the gland. It must, however, be kept firmly in mind that instead of pure *over-function* and pure *under-function,* we may in the

pathological cases be dealing with the complication of *perverted function* (dys-function), in which case the deductions drawn regarding normal thyroid function will require revision later.

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## 2. States of Over-function of the Thyroid Gland

*(Hyperthyreosis; Hyperthyroidismus)*

### (a) *Nature of Hyperthyroidism*

For nearly a century, clinicians have been interested in patients suffering from tachycardia, nervous symptoms, enlargement of the thyroid gland, and, often, though not always, with over-prominent eyes—a syndrome known in Great Britain as **Graves' disease,** in Germany as *Morbus Basedowii,* in Italy as *Morbo di Flajano,* and in France as *Goître exophthalmique.* At first classed with the neuroses allied to hysteria, the symptom-complex was, in 1886, ascribed by Moebius to a pathologically *increased activity of the thyroid gland,* a view that, though since extended to include the action of the excessive thyroid secretion upon the autonomic nervous system and the other endocrine glands, prevails at present. Something starts the thyroid gland into increased activity; it becomes enlarged through hyperplasia (*struma*), is very vascular and often pulsating (*struma pulsans*); the enlargement may cause local symptoms, but the phenomena of the disease depend, it is believed, chiefly upon the excessive

secretion causing (1) heightened excitability of the vegetative nervous systems, (2) secondary changes in the other endocrine glands, and (3) profound disturbances of metabolism.

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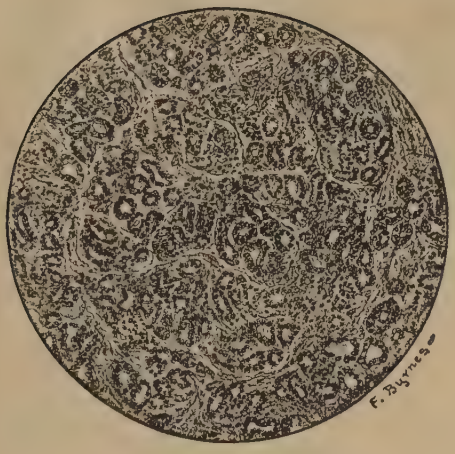
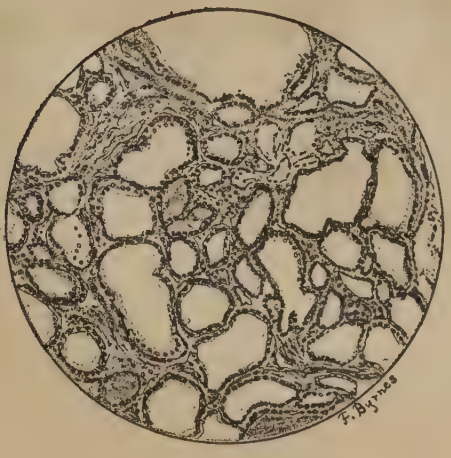
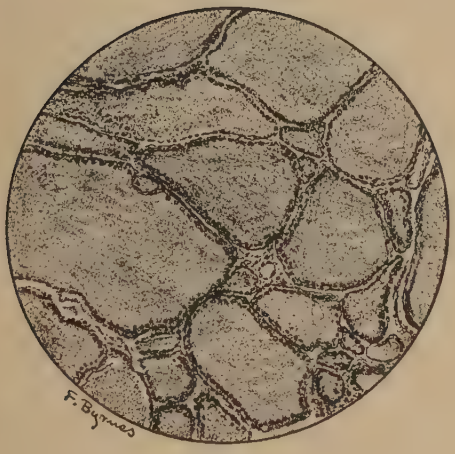


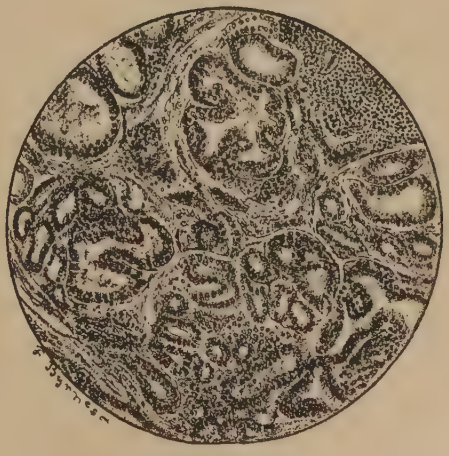
(*a*) Fetal Thyroid.



(*b*) "Normal" Thyroid.



(*c*) Cystic Thyroid.



(*d*) Hypertrophic Parenchymatous Goiter.

Fig. 647.—Cross-sections of Thyroid Gland. (After W. MacCarty, Collected Papers by the Staff of St. Mary's Hospital, Mayo Clinic.)

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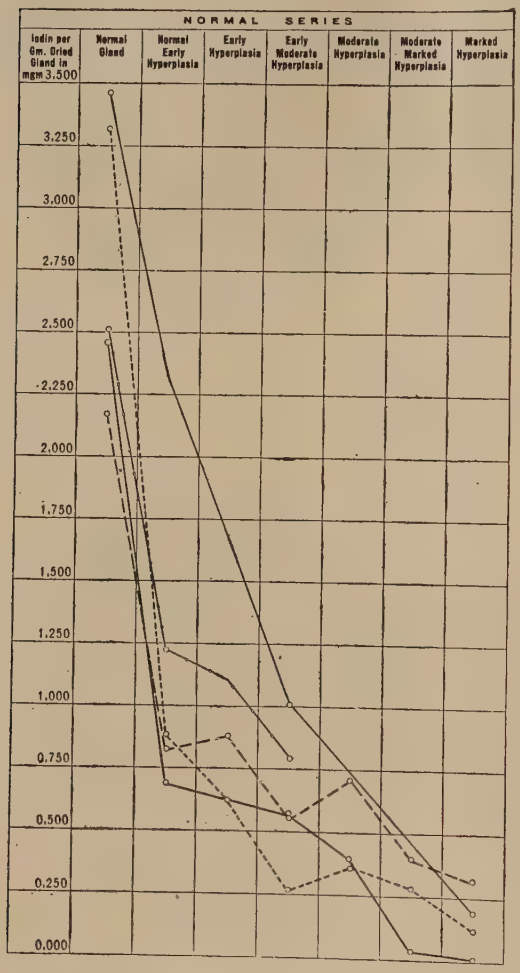


Fig. 648.—Curves Compiled from the Average Iodin-contents per Gram of Dried Gland of the Normal Series of Hyperplasias. The Solid Line Represents the Curve for the Ox, the Dotted Line the Curve for the Dog, the Line Composed of Short and Long Dashes the Curve for the Sheep, the Line with Short Dashes the Curve for Man, and the Line Composed of Long Dashes and Circles the Curve for the Pig. (After D. Marine and C. H. Lenhart, Arch. Int. Med.)

### (*b*) *Symptoms of Hyperthyroidism*

Aside from (1) the *struma* or *goiter,* the principal symptoms are referable to (2) the several domains of *autonomic innervation,* (3) the *metabolic processes,* (4) the functions of *endocrine glands* other than the thyroid, and (5) the *cerebrum.*

#### i. The Struma

The thyroid gland is nearly always enlarged, though often not perceptibly so in the early stages. The enlargement may involve uniformly the whole gland and give rise to a horseshoe-shaped goiter; or one lobe, especially the right, may be more enlarged than the other. The struma often shows ex-

pansile pulsation (*struma vasculosa*); bruits are audible over the thyroid arteries at the four poles of the gland; and a thrill is sometimes palpable. The surface feels granular; late in the disease the consistence is increased. The struma is tender on pressure, in contrast with colloid goiter. Exact measurements of the circumference of the neck, made at intervals, reveal frequent alterations in the size of the gland. The adjacent lymph glands are often slightly enlarged.

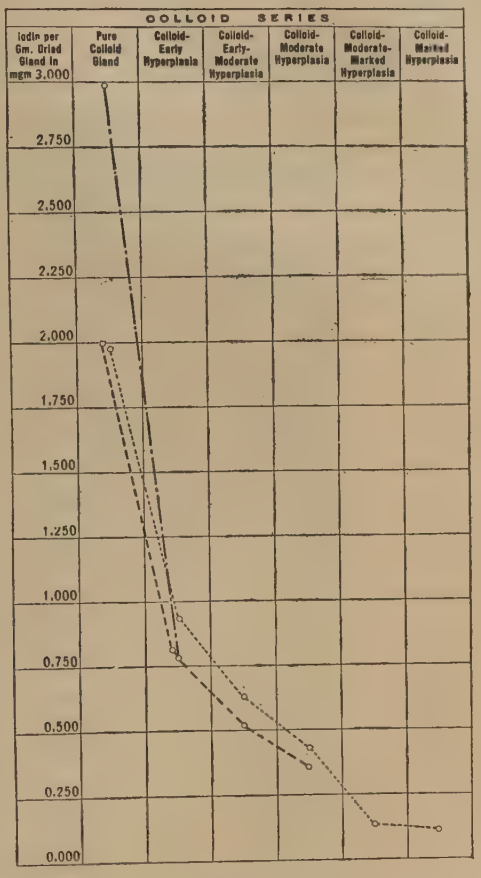


Fig. 649.—Curves Compiled from the Average Iodin-content per Gram of Dried Gland of the Colloid Series of Hyperplasias in Man, the Dog, and the Pig, Represented Respectively by Lines of the Same Character as in Fig. 648. (After D. Marine and C. H. Lenhart, Arch. Int. Med.)

If a portion of the gland be removed by a surgeon, *histological examination* reveals characteristic alterations. The tissues derived from Halsted's operations in the Johns Hopkins Hospital have been carefully studied by W. G. MacCallum. Wilson has made exhaustive reports from the Mayo clinic. To D. Marine of Cleveland we are also indebted for extensive studies of the pathological histology of the thyroid.

The basedowian struma is a *struma hyperplastica parenchymatosa teleangiectodes* (Kocher). The tissues are extremely vascular. The normal colloid is absent or greatly reduced in amount. The epithelial cells of the follicles undergo atypical proliferation; the cells assume the columnar type, arrange themselves in several superimposed layers, and often form papillalike projections, at first sight suggesting malignancy. Mitotic figures are common. The histological pictures resemble (1) those of the lactating breast (Greenfield), (2) those of compensatory hypertrophy of the gland following partial excision (MacCallum), (3) those commonly met with in the thyroids of dogs in Cleveland (D. Marine). The cytology of the thyroid with especial reference to the *secretion granules* has been carefully studied by R. R. Bensley. The lymphadenoid tissue of the gland is increased. In later stages, and especially after x-ray treatments, the interstitial connective tissue is increased, the capsule is thickened, and there may be firm extracapsular adhesions.

MacCallum made the important observation that these changes may, in some

cases, be limited to *islands* of the gland tissue. Areas of such hyperplasia are also met with in the glands of patients who, suffering from colloid goiter, eventually present signs of Graves' disease (*struma basedowificata*).

Recently, Emil Goetsch has made a careful study of the *mitochondria* in toxic thyroid adenomata.

When symptoms of Graves' disease are present and the thyroid does not seem to be enlarged, the explanation may lie in (1) a struma not recognizable before operation, (2) an insular change in the gland, or (3) an intrathoracic struma (x-ray).

Fig. 650.—Röntgenogram of Substernal Adenoma of the Thyroid. (After C. H. Mayo, Collected Papers by the Staff of St. Mary's Hospital, Mayo Clinic.)

The struma may cause local symptoms of *compression,* but much less commonly than does colloid struma; indeed if tracheal stenosis complicate Graves' disease, the case is usually one of colloid struma that has become "basedowified."

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### ii. The Symptoms Referable to Disturbances of the Autonomic Innervations

These include all the symptoms referable to abnormal innervations of the smooth muscle, cardiac muscle, and secreting glands of the body; they may also include some of the disturbances of metabolism, but these will be considered under a separate heading.

The abnormal autonomic innervations may most conveniently be considered by regions, (1) eyes, (2) cardiovascular system, (3) skin, (4) digestive system, (5) respiratory system, (6) urogenital system.

In hyperthyroidism, the abnormal autonomic innervations concern both the sympathetic and the craniosacral (or so-called vagal) systems. In some patients (sympathicotonic) symptoms referable to the sympathetic system predominate; in other patients (vagotonic) symptoms referable to the craniosacral autonomic system are most prominent; in still other patients, the symptoms may almost equally concern the two systems (mixed cases), and it would seem that in this third group, mental symptoms are prone to be more severe (Eppinger; v. Noorden, Jr.; Barker and Sladen).

### (1) *The Eye Signs of Graves' Disease*

Most of these are autonomic in origin; a few have other sources. The most important eye signs are (1) protrusion of the eyeballs, (2) widened lid-slits or Dalrymple's sign, (3) the dissociation between the movement of the eyeball and the upper-lid or v. Graefe's sign, (4) the insufficiency of convergence or Moebius' sign, and (5) the infrequency and incompleteness of involuntary winking or Stellwag's sign. Among the minor eye signs may be included (6) swollen lids or Gifford's sign, (7) the glistening eye, (8) anisocoria, (9) epinephrin-mydriasis or Loewi's sign, (10) epiphora, (11) dry eyes, (12) pigmented eyelids or Jellinek's sign, (13) tremor of the closed eyelids or Rosenbach's sign, (14) subjective feelings of heat or pain in the eyeballs.

**Protrusion of the Eyeballs** (*protrusio bulborum*), best seen on examining a patient in profile, may or may not be accompanied by widened lid-slits. Usually symmetrical, the protrusion may be unilateral, or, at least more marked on one side than on the other, and then most often, though not always, on the side that corresponds to the more enlarged lobe of the thyroid gland. Protrusio bulbi is not a constant sign in Graves' syndrome; probably not over 1/3 of the patients manifest it. When it does occur, it is usually a late manifestation, though in some instances, especially in "hyperthyroid families," it may exist for years, even from childhood, before any other symptoms of the complex become manifest. It may develop suddenly; I saw a man in Chicago who 24 hours after a heavy loss in the stock market suffered sudden and severe protrusio bulborum, together with other severe manifestations (*hyperthyroidismus peracutissimus*).

For a time after its appearance, the protrusion is variable in intensity; the eyeball can be pushed back by gentle pressure. Later on, fat tissue in the orbit may fix the eyes in their protruded positions.

Protrusio bulbi should be sharply distinguished from the appearance due simply to widened lid-slits; the two conditions are often confused.

The term *exophthalmos* has been loosely used to mean one or the other, and it is best avoided. There is still much dispute as to the mechanism of protrusio bulbi; despite the objections raised to the view, I still lean to the explanation that assumes an increased tonus of the smooth muscle of the septum orbitale (Landström), innervated by the sympathetic.

**Widened Lid-slits** (*Dalrymple's Sign*).—This may be obvious when the eyes are at rest; it is often exquisitely demonstrable by asking the patient suddenly to fix the eyes on an object held before them, the upper lid undergoing a pronounced retraction with exposure of the sclera above the cornea on fixation. This sign is independent of protrusio bulbi; when present with slight protrusion it may lead to an exaggerated estimate of the degree of protrusion. Widened lid-slits appear to be due to an abnormally high tonus in the M. levator palpebrarum, maintained by fibers of the craniosacral autonomic system running in the N. oculomotorius. Some reserve the term "Dalrymple's Sign" to designate the sudden widening of the lid-slit in fixation.

**Dissociation of the Movement of the Eyeball and of the Upper Eyelid** (*v. Graefe's Sign*).—In Graves' disease, a very common sign is a disturbance of the associated movement of the upper lid with the eyeball on looking downward, so that the lid does not follow the eyeball down as normally, but is held back, owing to an abnormal tonus in the M. levator. It is surprising how often this sign will be found positive if it be systematically looked for, even in cases without other symptoms of hyperthyroidism. In the absence of other symptoms, too much stress should not be laid upon it.

**Insufficiency of Convergence** (*Moebius' Sign*).—Many hyperthyroid patients manifest this sign. When the patient is looking straight before him at the examiner's finger, if this be gradually moved toward his eyes, instead of maintaining the eyes in the convergence-position, one or the other eye will soon move lateralward, leaving only one eye looking at the finger, strange to say, *without* diplopia.

One must make sure that the patient is not myopic, for, in a myopia of more than 10 diopters, one always meets with this sign. Moebius' sign is also sometimes seen in neurasthenic states other than those accompanying hyperthyroidism. It does not appear to have an autonomic origin.

**Infrequency and Incompleteness of Involuntary Winking (Stellwag's Symptom).**—Normally, involuntary winking occurs from three to ten times per minute. In Graves' syndrome, it may occur much less frequently, sometimes only once in several minutes. The sign is positive in 30 to 50 per cent of the cases.

Stellwag's name has also been applied to widened lid-slits, but to avoid confusion this is better avoided.

**Explanation of the Minor Eye-signs.**—The *glistening eye* and *epiphora* are due to increased lachrymal secretion (vagotonic signs), the *dry eye* to lessened secretion, and the epinephrin-mydriasis to heightened tonus in the M. dilator pupillae (both sympathicotonic signs). *Anisocoria* indicates a disturbance of balance between sympathetic and craniosacral autonomic innervation of the pupillary muscles on one side. The *pigmentation of the eyelids* is probably due to a disturbance in the chromaffin system.

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### *(2) The Cardiovascular Symptoms of Graves' Disease*

**Tachycardia.**—Of all the signs of Graves' disease, *tachycardia* is the most constant. When the hyperthyroid syndrome is well-developed, the pulse rate may vary between 100 and 180 per minute. Emotional excitement increases the rate, even more than physical exertion. *A persistent tachycardia is often the first symptom to call the attention of the physician to a developing Graves' disease.* I have learned to regard with suspicion, in the absence of acute and chronic infections, all pulse rates that persistently remain above 80-85 per minute. In "rest cure" patients, it is not uncommon to see an initial bradycardia (60-65) go over, on rest in bed and over-feeding, into a tachycardia (80-100), thus unmasking a thyropathy often partly responsible for the "nervous breakdown." The tachycardia is due to stimulation of the N. accelerator. It is more marked in sympathicotonic cases, less marked in vagotonic patients. The *electrocardiogram* shows a curve precisely like that obtained during physical exercise.

**Palpitation.**—The subjective feeling of *palpitation* may be very distressing. It is largely independent of the pulse rate, being often less marked in cases with very rapid pulse than in those with slight tachycardia.

**Other Vascular Signs.**—The *heart* is often moderately dilated (orthodiagram); accidental murmurs may be audible, especially over the bases. The *carotids* and *brachials* may pulsate violently, almost as in aortic insufficiency. The *blood pressure* is usually low, though the Graves' syndrome may occur also in patients with arterial hypertension.

A *pulsus irregularis respiratorius* is often met with. *Vasomotor abnormalities* are frequent; they include temporary erythemas, especially of the neck and upper thorax, dermographism, urticaria, pruritus, and subjective feelings of heat.

While the above symptoms are largely autonomic in origin (cardiac nerves; vasomotor nerves), the *heart muscle* also suffers in prolonged thyreo-intoxication. Late in the disease, *myocardial insufficiency* may develop and lead to exitus. I have often observed a *pulsus irregularis perpetuus, with auricular fibrillation,* in the electro-cardiogram in long-standing cases of thyreo-intoxication.

Fig. 651.—Hyperthyroidism, Terminal Results: Chronic Toxemia not Abated, but Leaving Myocardial and General Degenerative Changes. (After C. H. Mayo, Collected Papers by the Staff of St. Mary's Hospital, Mayo Clinic.)

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### (3) *The Cutaneous Symptoms of Graves' Disease*

In hyperthyroidism, the skin is usually *thin, delicate, soft* and *moist* (contrast with myxedema). Besides the vasomotor phenomena already referred to, *profuse sweating* is a common and troublesome symptom. It is usually general, but may be unilateral or localized. The increased secretion of sweat is responsible for the lessened resistance of the skin to the electric current (*Vigouroux's sign*).

The skin is often abnormally *pigmented*, owing probably to an associated disturbance of the chromaffin system. The pigmentation may be general, but is more often localized, especially about the eyelids, nipples, axillae, and genitals.

In some cases *localized myxedemalike swellings* of the skin occur. The *hair* sometimes falls out (scalp, eyebrows, beard, axillae, genitals). The *nails* are usually long and tapering; occasionally they show trophic disturbances.

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### (4) *Symptoms Referable to the Digestive Apparatus in Graves' Disease*

The *saliva* may be over-abundant (vagotony), or scanty (sympathicotony). Far more important are (1) the *vomiting,* and (2) the *unmotived* attacks of watery, painless *diarrhea* (4-8-30 stools per day), symptoms often very intractable, and leading to rapid emaciation.

These symptoms may appear suddenly and stop just as suddenly, without apparent reason for either onset or cessation. The diarrhea often alternates with *spastic constipation.* Independent of the basedowian diarrhea, *fatty stools* may be met with; they depend upon a disturbance of absorption, not upon faulty fat-splitting. *Icterus* is rare.

### (5) *Symptoms Referable to the Respiratory System in Graves' Disease*

The symptoms in the respiratory system depend upon stimulation of the visceral nerves; they include: (1) *shallow-breathing* (Bryson's sign), (2) *tachypnea,* (3) *subjective feelings of dyspnea,* and (4) *asthmatic attacks.* It must be kept in mind that dyspnea and cough may sometimes depend upon local pressure due to the struma (*tracheal stenosis, recurrens paralysis*), though such pressure is more common in colloid goiter.

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### (6) *Symptoms in the Urogenital System in Graves' Disease*

The close relation of the thyroid to the female genitalia has long been recognized through the swelling of the thyroid at puberty and in pregnancy. Graves' disease is much more frequent in women than in men.

In hyperthyroidism, menstrual disturbances are frequent. Thus there may be *amenorrhea,* or scanty flow, or, less often, *menorrhagia.* The *breasts* may early hypertrophy, or they may, in Graves' disease, look virginal in middle life.

In men, there may be disturbances of *libido* and of *potentia.* In both sexes, *genital hypoplasia* is not infrequently associated with Graves' disease; we have then to think of a general involvement of the endocrine glands (hyperthyrosis, hypogenitalismus, hypopituitarism, status thymicus, etc.).

*Polyuria* is a frequent symptom; occasionally, there is *oliguria. Polliakiuria* may be a troublesome phenomenon at times in the course of the disease.

### iii. Disturbances of Metabolism in Graves' Syndrome

Rapid *emaciation* despite a large food intake and, often, without obvious disturbance of digestion was long a puzzling phenomenon in Graves' disease until Fr. v. Müller (1893) demonstrated the great *acceleration* of the metabolic processes accompanying the condition. Many studies have since been made, and we know now that the disturbances involve the total combustion, and the protein, carbohydrate, fat and mineral metabolism.

**Total Metabolism.**—The *total combustion* ($CO_2$-production and $O_2$-consumption), in the fasting-resting state may be 50 per cent to 70 per cent greater than normal. Instead of the 3.5-4.0 c.c. of $O_2$ per kg., the values may rise to 4.5-6-7 c.c. (Magnus-Levy). The fires of the body are, as it were, fanned into an intense flame. A patient with hyperthyroidism may, at rest, use as much oxygen in his combustion as a normal man at hard labor. This acceleration of the oxidative processes may over-tax the

heat-regulatory mechanism; thus slight elevations of the body temperature frequently accompany the syndrome.

**Protein Metabolism.**—The protein metabolism is distinctly accelerated and N-equilibrium is maintained only with difficulty; in the severer cases, the toxic destruction of protein becomes very obvious (see *Cachexia*).

**Carbohydrate Metabolism.**—The carbohydrate metabolism also may show abnormalities. Spontaneous glycosuria occasionally occurs, though it is not common. In many cases, however, an alimentary glycosuria is demonstrable, disappearing when the disease is cured.

A combination of Graves' disease with true diabetes mellitus occasionally occurs.

**Mineral Metabolism.**—Attention has been directed to certain possible disturbances of mineral metabolism in the thyro-intoxications. There is often a loss of *phosphorus*, especially through the intestine (W. Scholtz); this appears to be related to an increased excretion of *calcium* by way of the feces (Falta). For a study of the calcium and magnesium in some of the cases under my care, the work of Caroline Towles may be consulted.

The observation that only small amounts of *creatinin*, both endogenous and exogenous, are excreted in the urine in Graves' disease (Forschbach) awaits explanation.

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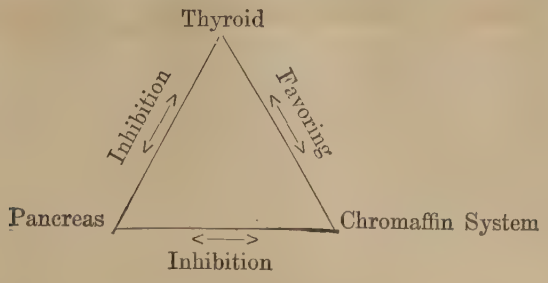
## iv. Symptoms in Graves' Disease Due to Disturbances of Endocrine Glands Other than the Thyroid

The interrelations of the various endocrine glands of the great hormonopoietic system have recently been the object of serious studies, and a mass of facts has been accumulated, though it must be admitted that theories as yet almost outnumber facts.

Brief reference only to the topic is permissible here. It is to the younger school of clinicians in Vienna (Eppinger, Falta, Rüdinger, v. Noorden, jr.) that we owe many of the facts and hypotheses relating to this field. Their experiments were undertaken to ascertain, if possible, in how far given hormones act, directly, upon the visceral nervous system, and in how far, indirectly, through the intermediation of other endocrine glands. Since objective measurements could most easily

be applied to changes in metabolic processes, it was to these processes that their experiments were directed. Their results are best illustrated by the accompanying diagram:




As far as metabolic experiments go, the thyroid and pancreas on the one side, and the pancreas and the chromaffin system on the other, mutually inhibit one another's activities. Reversely, the thyroid and the chromaffin system reciprocally favor each other's activities, an under- or an over-function of the one gland leading to an under- or an over-function of the other. If this view be correct, then hyperthyroidism must lead to an insufficiency of the internal secretion of the pancreas and to increased activity of the adrenals, while hypothyroidism must lead to overfunction of the pancreas and to diminution of adrenal activity.

These investigators think that the glycosuria of Graves' disease is an indirect effect through the chromaffin system, and that the hyperexcitability of the sympathetic nervous system in the syndrome as shown by epinephrin-mydriasis is to be similarly explained. Indeed, the **sympathicotonic cases** of Graves' disease, with the symptoms of protrusio bulbi, negative von Graefe, positive Loewi, positive Moebius, dry eyeballs, great tachycardia, dry skin, constipation, falling hair, slight fever, eosinopenia, and alimentary glycosuria, they attribute to thyrogenic over-activity of the chromaffin system; and to explain the **vagotonic cases** with the symptoms of relatively slight tachycardia, marked subjective feelings of palpitation, outspokenly positive von Graefe, wide lid-slits, negative Moebius, slight or absent protrusio bulbi, epiphora, sweats, diarrheas, gastric hyperacidity, eosinophilia, lymphocytosis, pulsus irregularis respiratorius, and unlessened carbohydrate tolerance, they assume the existence, in the thyroid secretion, of a component (pharmacologically resembling the vagotropic drugs pilocarpin and muscarin) that has an especial affinity for the craniosacral autonomic nervous system, and which can be neutralized in part at least by an antagonistic vagotropic drug; viz., atropin.

So speculative are these views that many workers are violently opposed to their consideration. Meltzer and others have opposed especially the use of diagrams such as the above, since they fear that those unfamiliar with the subject will take for fact what is as yet merely hypothesis.

It is well worth while, however, as my own studies have convinced me, in every case of Graves' disease to analyze the symptoms with reference not only to the endocrine functions of the thyroid gland, but also with reference to the functions of the pancreas, the adrenals, the genitals, the thymus, the hypophysis, etc. Though such analyses may not permit of other than a suspended judgment in many of the cases, they are always

instructive, and often lead to the discovery of anomalies and relations that might otherwise be entirely overlooked.

Recently, attention has been repeatedly drawn to the fact that many of the patients suffering from Graves' disease are also thymus carriers. In some cases of Graves' disease, thymectomy without thyroidectomy may be followed by marked subjective and objective improvement.

The Basedow thymus has been carefully studied histologically. Investigators have found marked hyperplasia of the medulla of the gland, the presence of many Hassall's corpuscles, and accumulations of eosinophils along the septa of the gland and along the blood vessels.

Capelle and Bayer believe that both the thyroid gland and the thymus gland produce an internal secretion that has two components, one sympathicotropic and one vagotropic. They suggest that in the Basedow thymus the eosinophilic accumulations in the gland correspond to a vagotropic secretion, while marked hyperplasia of the epithelioid elements of the gland corresponds to a sympathicotropic secretion. Similarly, histological differences corresponding to sympathicotropic and vagotropic secretions they think can be made out in the thyroid. They believe that variations in the proliferation in both the thyroid and in the thymus will account for the manifold types of Graves' disease met with clinically. The thyroid effect is on the whole predominantly sympathicotropic, whereas the thymus effect is predominantly vagotropic.

Some observers believe in the possibility of a Graves' disease due to primary disease of the thymus. It is said that a thyro-intoxication leads to hyperplasia of the thymus, and a thymus intoxication leads to enlargement of the thyroid. The effects of the thymus and of the thyroid on other endocrine glands may be antagonistic; thus, in the development of the tadpole Gudernatsch has shown that thyroid feeding causes dwarfism with greatly accelerated differentiation, while thymus feeding causes gigantism with slow differentiation.

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### v. Cerebral Symptoms in Graves' Disease

Nervous and mental symptoms are very common in this syndrome; indeed, in *neurasthenic states* and in *mild mental disturbance* the physician should always think of the possibility of hyperthyroidism as a factor.

There is a kind of *apprehensiveness* and *anxiety* that is especially common, and *phobias* and *obsessions* are also frequently present. Many patients complain of *insomnia.*

Aside from these milder symptoms, *outspoken psychoses* are sometimes met with (manic-depressive type, dementia precox, paranoid states).

Whether the **tremor,** so characteristic of the disease as to be classed by Charcot as a *fourth cardinal symptom* (along with the tachycardia, the struma and the exophthalmos = *Mersenburger Trias*), is to be regarded as a cerebral symptom or not is uncertain. A large percentage of the cases exhibit tremor, though it is not present in all. The tremor is *fine* and *rapid* (7 to 10 oscillations per second), though this fine tremor is sometimes accompanied by coarser oscillations, especially on excitement. It is best visible in the fingers when the upper extremity is outstretched rigidly from the shoulder and the fingers held wide apart. It is sometimes present in the toes. The patient may have been unaware of the tremor before examination.

Other symptoms referable to the cerebrum (*epileptiform convulsions, paralyses*) are probably to be regarded as complications rather than as direct symptoms. I have, however, studied several cases of epilepsy in which thyro-intoxication seemed to be an important etiological factor.

The pronounced *myasthenia* occasionally met with may also be cerebral in origin; it may, on the other hand, be, like myasthenia gravis, associated with the thymus hyperplasia commonly present in Graves' disease.

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### vi. The Blood Picture in Graves' Disease

The *red count* may be normal and the *absolute white count* may be unchanged except for a slight leukopenia. The *differential count,* how-

ever, often shows characteristic alterations in the form of an outspoken **lymphocytosis** (35-60 per cent), with corresponding *neutrophilic leukopenia.* Occasionally there is also *eosinophilia.* Recent studies support the view that the lymphocytosis may be due to *status thymicolymphaticus,* which so frequently accompanies the Basedow syndrome. Klose believes that the thyro-intoxication leads to hypogenitalismus, and that this in turn causes the status thymicolymphaticus with lymphocytosis.

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### (c) *Etiology of Graves' Disease*

This is far from clear. My own studies indicate that *hyperthyroidism has no unitary origin* but may be the result of changes in different parts of the body, especially of changes that cause *irritation in some domain of the vegetative nervous system* (sinus infections, tonsillar infections, pulmonary infections, infections of the digestive tract, infections in the urogenital organs). In some cases, *fright,* extreme *emotional excitement,* or a *physical trauma* may suddenly precipitate the syndrome. In other cases, the onset is *insidious.* Certain *infections* (influenza, polyarthritis rheumatica) seem especially to predispose. *Iodin therapy* and *thyroid extract therapy* have called forth the symptoms in some patients. Infections involving the thyroid gland itself (*thyroiditis*) and *tumors in the thyroid* may be followed by the signs of Graves' disease.

I have been struck with the frequent occurrence of Graves' disease in *families. Women* are more often affected than men, in the proportion of 4 or 5 to 1. The syndrome develops as a rule in *early life* (15th to 35th year), but may be met with in childhood, or in later life. I have seen it in women over sixty, though, often, when the syndrome has been present before the menopause, the symptoms become less marked afterward.

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### (d) *Typical and Atypical Cases of Graves' Disease*

When three or four of the cardinal symptoms (tachycardia, struma vasculosa, protrusio bulborum, tremor) are present the cases are designated as *typical;* in less complete forms, in which only one or two of the chief symptoms are manifested, the cases are classed as *atypical* or *formes frustes.*

Now that our knowledge of the autonomic nervous system has been so greatly increased, we must be more cautious than formerly in deciding that a given case with incomplete symptoms is really due to hyperthyroidism, for we now know that many of the symptoms met with in Graves' disease may be due to disturbances in other endocrine glands, or to irritations in local domains of the autonomic system. Thus, tachycardia and adrenalin-glycosuria, on the one hand, and sweats, diarrheas, pigmentations, lymphocytosis, eosinophilia, on the other, may occur in the entire absence of thyropathy. Unless there is struma and increased vascularization of the thyroid gland (bruits), one should be cautious in assuming that the symptoms are due to hyperthyroidism.

The so-called **goiter heart** (*cardiopathia thyrotoxica*), though as a rule due to thyro-intoxication, may sometimes depend upon pressure upon the vagi in the neck. In the latter cases, it is known as *Rose's goiter heart,* or the *dyspneic form of goiter heart.*

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### (e) *Diagnosis of Graves' Disease*

In the *typical cases* (*vide supra*), no difficulty will be encountered. The vascular struma, the tachycardia, the tremor, the disturbances in the vegetative nervous system, including the eye-signs, the nervous and mental state, the metabolic disturbances, and the blood picture, leave no room for doubt. In the *atypical cases* (*formes frustes*) great difficulty may be experienced in forming a judgment. Cases of undoubted Graves' disease are very frequently overlooked by the general practitioner, and mistakes are sometimes made even by the best diagnosticians with a large experience in the syndrome. We can scarcely do better than to urge the practitioner to *think* of the possibility of hyperthyroidism in every case in which he meets with (1) *tachycardia,* (2) *rapid emaciation,* (3) *excessive sweating,* (4) persistent *watery diarrhea* without apparent cause, (5) *neurasthenic state,* (6) outspoken *lymphocytosis,* (7) one or more of the *eye-signs,* and (8) *fine tremor.*

At the same time, a word of caution is necessary lest a diagnosis be made upon insufficient grounds, since any one, or even several, of these manifestations may be due to conditions other than hyperthyroidism.

When there is difficulty in diagnosis, Reid Hunt's *acetonitril test* may be helpful, since, in definite hyperthyroidism, a white mouse fed with the blood of the patient acquires an increased resistance against acetonitril intoxication.

A determination of the *epinephrin-content of the blood* by the method of A. Fraenkel, or by the method of Folin, may also be helpful, since in the outspoken syndrome, the adrenalin content is said to be high. Unfortunately, in the atypical cases, neither the acetonitril test nor the epinephrin test is often positive. These tests are, therefore, of but little practical help as yet in differentiation.

Plummer, who has had a large experience at the Mayo clinic, reserves the term "exophthalmic goiter" for cases running a certain definite course, associated with parenchymatous hyperplasia of the thyroid gland.

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### (*f*) *Complications of Graves' Disease*

The synodrome is frequently complicated by other disturbances, (1) of certain endocrine glands (diabetes mellitus, myxedema, tetany, acromegaly, Addison's disease, osteomalacia); (2) of the nervous system (hysteria, epilepsy, chorea, paralysis agitans, psychoses); and (3) by severe cardiopathies (especially auricular fibrillation), or nephropathies.

### (*g*) *Diagnosis of Indications for Operation in Graves' Disease*

The physician has often to decide whether or not *strumectomy* is to be performed.

In cases in which the mechanical compression from the struma (usually cases of struma basedowificata) is doing harm, there would be no hesitation in recommending operation. Again, in the typical syndrome, when there is no favorable response to a few weeks of good medical treatment, operation should be advised unless the state of the heart or kidneys contraindicates it. The doubtful cases are (1) those that improve on medical treatment without getting well, and (2) the so-called atypical cases. Here the judgment of the internist will often be severely taxed. We need better criteria than we have at present for making a decision. Our surgical colleagues should certainly be permitted to see the cases early, before thyro-intoxication has gone on for a long time.

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## 3. States of Under-function of the Thyroid Gland

(*Athyreosis, Hypothyreosis, Hypothyroidism*)

### (*a*) *Introduction*

In states of under-function of the thyroid, we have to deal either with complete loss of the thyroid substance (*athyreosis*), or partial loss of the same (*hypothyreosis*), both of which lead to *hypothyroidism*. The best example is the state following removal of the thyroid gland by operation, the so-called *operative myxedema* or *cachexia strumipriva*. A similar condition may arise in adult life, due to retrogressive changes in the thyroid gland (*idiopathic myxedema*), or in childhood and youth, from failure of the thyroid gland to develop (*thyro-aplasia, congenital myxedema*). Closely related to these cases are the cases of (1) *endemic cretinism*, and (2) cases of *slight hypothyroidism* (Kocher's *thyropenia*), which, not presenting the outspoken signs of myxedema, are often overlooked by physicians.

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## (*b*). *History of Myxedema*

Myxedema is the main symptom in the following forms of hypothyreosis: (1) *operative myxedema,* (2) *idiopathic myxedema of adults* or *Gull's Disease,* and (3) *congenital* and *infantile myxedema.*

Our knowledge of myxedema dates from 1873 when Sir William Gull pointed to the idiopathic condition in adults, calling attention to the peculiar leatherlike

Fig. 652.—Myxedema, Infantile, Age 29. (*a*) Front View; (*b*) Profile View. (Med. Service, J. H. H.)

skin and the mental stupidity. Two years later Wm. Ord reported several similar cases, to which, later on, he gave the name *myxedema* on account of the mucuslike edema of the skin found at autopsy. Ord observed changes in the *thyroid gland* in one of his cases at the post mortem, but emphasis upon the small thyroid in myxedema was first laid by Hadden (1882). In 1881 Charcot recognized the identity of myxedema with cases described earlier by him as *cachexia pachydermique.* The important report made by Kocher (1883) first called attention to the *cachexia strumipriva* following operations for goiter in which the whole thyroid gland had

been removed, and in the same year was published the important paper by Reverdin on *myxedème postoperatoire.*

In 1888, the Myxedema Commission of the Clinical Society of London made its report, in which it was asserted that the thyroid gland has an unexplained chemical function bearing upon normal growth and the normal function of other organs. In the report it was maintained that genuine *myxedema* and so-called *sporadic cretinism* are identical with one another and essentially the same as the *cachexia strumipriva* due to loss of the physiological function of the thyroid gland resulting from thyroidectomy. The inconstancy of the appearance of myxedema after total extirpation was shown to be due to the frequent occurrence of *accessory thyroid glands,* and the occasional occurrence of outspoken myxedema after partial extirpation was interpreted as due to defective function of the part of the thyroid gland not removed.

Schiff, Victor Horsley and von Eiselsberg showed the possibility of preventing myxedema by transplanting the thyroid gland in animals, a fact confirmed for human beings, later on, by Kocher and Bircher.

A further advance in our knowledge of the subject was scored when Murray showed that operative myxedema can be prevented by the administration of extract of thyroid gland subcutaneously. Later, Hector Mackenzie (London) and Howitz (Copenhagen) showed that the same result can be attained by administration of the thyroid gland by mouth. Soon after this, the beneficial effects of thyroid-administration in myxedema and in cretinism were demonstrated.

The difference between *ordinary endemic cretinism* associated with goiter and with family cretinism and so-called *sporadic cretinism* due to congenital thyroaplasia was clearly shown by Pineles (1902), since when the term sporadic cretinism has given way to a better designation—*congenital myxedema.* Comparatively recently, too, *infantile myxedema,* responding favorably to thyroid therapy, has been separated from congenital myxedema with which it was formerly classed. At present, clinical studies are largely directed toward (1) the differentiation of the *growth disturbances due to the thyroid* from other growth disturbances independent of the thyroid (chondrodystrophia fetalis; Mongolismus; dwarfism with idiocy), and (2) the atypical and latent forms of hypothyreosis, the so-called *myxedème fruste* or *thyropenia* of Kocher.

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### (*c*) *Symptoms in the Myxedematous States*

The symptom *myxedema* is common, as we have seen, to three different forms of hypothyreosis: idiopathic myxedema, operative myxedema, and congenital myxedema.

#### i. Changes in the Common Integument in Myxedematous States

The condition of the skin is characteristic. It is thickened, dry, rough and often thrown up into folds.

The color is pale and waxy, though in later stages it may be pigmented, especially on the upper arms, on the legs, and about the eyes and mouth.

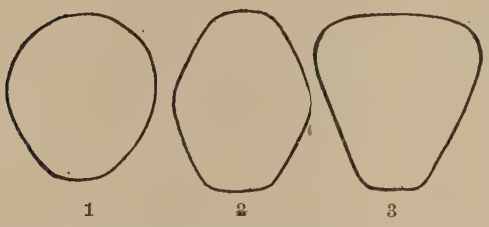


Fig. 653.—General Contour of the Face in: 1, Myxedema; 2, Acromegaly; 3, Paget's Disease. (After Pierre Marie in A. Léri's article in "Hand. d. Neurol.," published by J. Springer, Berlin.)

The most marked changes are met with in the skin of the head and of the hands. The scalp is easily movable. The *face* looks edematous, but does not pit on pressure; the *sacs below the eyes* suggest, at first glance, the edema of nephritis. Similar swellings occur beneath the chin, and about the lips, cheeks and eyebrows. The little folds of the skin are not obliterated as in genuine edema. The *wrinkles of the forehead* are exaggerated, and may call attention to the condition. The *double chin* and *the pads of fat above the clavicles* are very characteristic. Similar masses in the subcutaneous tissue may occur in different parts of the body.

The *hands* are short and plump, and suggest the appearance of mittens (Ewald). The dorsum of the *foot* is similarly swollen. The skin may be thrown up into thick folds on the anterior *abdominal wall,* and about

the *hips* the fatty deposits often assume an angular shape, disagreeable to look at. The normal contour of the ankles is often obscured.

The *hair* is short and tends to fall out. The *nails* break easily and show longitudinal grooves. The *teeth* are often carious.

Subjectively, the patients complain of a *feeling of weight* in the limbs and of a *tight feeling* in the hands. They nearly always feel *cold*, even in warm weather; though their hands and cheeks may look red, they are cold and dry to the touch.

Fig. 654.—Loss of Contour of Ankle in Myxedema Following Goiter. (Med. Service, J. H. H.)

### ii. The Thyroid Gland in Myxedema

On palpation, this gland can rarely be felt, or, if felt, it is found to be small. There is no tenderness on pressure.

### iii. Nervous Symptoms in Myxedematous States

The patients are *slow* of speech and the *voice* is indistinct and monotonous, due less to thickening of the tongue than to the mental state. The patients complain of *feeble memory and slowness of thought.* They lack energy and initiative and find it hard to dress, undress, and perform the ordinary movements of life. In the severest forms, the *slow, clumsy movements,* the monotonous speech and the *stupid appearance of the face,* with sleepy looking eyes, make one think almost of idiocy.

The *reflexes* are unchanged. Many patients complain of dimness of vision, though it is rare to find objective changes in the eye-grounds.

In experimental animals, removal of the thyroid gland prevents regeneration of medullated nerves, but if thyroid gland be fed to such animals the regeneration goes on promptly (Walter).

### iv. Metabolic Disturbances in Myxedema

As might be expected, metabolism is affected in a way exactly opposite to that of Graves' disease. *All the metabolic processes are slowed.*

The *total metabolism* (calories) is much less than normal. The oxygen

consumption is reduced by 50 or 60 per cent, so that a patient with a food intake small in calories can maintain a normal weight.

The *protein metabolism* is also slowed, and the amounts of total nitrogen, urea and uric acid excreted are less than normal. The output of these substances can be rapidly increased by administering thyroid extract (without change in the diet).

The *mineral metabolism* has been studied, but with, as yet, conflicting results.

The *carbohydrate tolerance* is markedly heightened, no alimentary glycosuria appearing after the ingestion of 200-300 g. of d-glucose. The occasional glycosuria met with in myxedema is not explained.

The amount of *water* given off by the skin and by the breath (perspiratio insensibilis) is markedly reduced, and there may be moderate oliguria. It is said that the *excretion of methylene blue* is slowed in myxedema and that its excretion in such cases can be markedly heightened by feeding thyroid tablets (Garnier and Lebret).

### v. Growth Disturbances in Myxedema

In myxedema of young people, the *growth of bone* is markedly interfered with. The phenomena in the bony system, in a given case, depend upon the time of life when the thyroid function began to fail. In *congenital* and in *infantile myxedema,* there is a delayed growth of the bones, especially of growth in the longitudinal direction. The *ossification centers* at the wrist and ankle fail to appear. By consulting Dieterle's table, one can tell, by x-ray examinations, at what stage the growth of bone became inhibited from failure of the thyroid function.

It is the *endochondral* bone formation, rather than the membranous bone formation, that is affected. This accounts for the *macrocephalic skull* of juvenile myxedema.

### vi. Other Symptoms in Myxedematous States

The *pulse,* as a rule, shows no marked changes; it may be either slightly slowed or slightly accelerated. *Arterial thickening* tends to occur early. The *blood pressure* is usually low. *Vasomotor reactions* are sluggish.

The *temperature* is often subnormal, though when myxedema is complicated by infection, the temperature rises as usual.

In the digestive system, the *large tongue* and the *dry mouth* are striking features. Intractable *constipation* is an important symptom.

*Amenorrhea* in the female, and *impotence* in the male, are common symptoms. If the thyroid be deficient during the developmental period, the genitalia fail to develop properly.

In the *blood* there is often leukopenia and a moderate eosinophilia, sometimes a lymphocytosis. The coagulation-time is accelerated (in contrast with the retardation in Graves' disease) and the fibrin-content of the blood is increased. *Albuminuria* is common when the myxedema has lasted for a long time.

### vii. Complications of Myxedema

It is not uncommon to find myxedema associated with diseases of other endocrine glands (acromegaly, pigmentations); occasionally myxedema and Graves' disease occur together.

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### (*d*) *Idiopathic Myxedema* (*Gull's Disease*)

This condition, appearing most frequently in the *third decade* of life, and more often in *females* than in males (113 : 32, Prudden), usually begins with *thickening of the skin* of the face, sometimes associated with *neuralgic pains.* Later, the skin of the arms and legs becomes affected. The *onset* is, as a rule, insidious, over a period of years, though in some cases the changes may occur rapidly; in certain instances, full-blown myxedema may develop within a few weeks. In the cases of insidious onset the patients are often treated for neurasthenic states before the underlying malady is discovered. Vague pains in the muscles are common.

### (*e*) *Operative Myxedema*
(*Cachexia thyropriva*)

If the thyroid be removed *in toto,* an operation performed very rarely by surgeons nowadays, though it was not infrequently done a few years ago, *cachexia strumipriva* quickly develops. The patients become extremely *dull;* they complain of *tiring easily,* and say that their hands and feet *feel cold.* Speech and thought are slowed in marked contrast with the former powers of the person. The *skin* begins to swell, the changes being more marked on waking in the morning than later in the day. The swellings are transitory at first. The *hair* begins to fall out, and *cachexia,* with pallor and oligocythemia, develops. The occurrence of *tetany* as a complication is due not to the lack of thyroid, but to the simultaneous removal of the parathyroid glands.

If the thyroid be incompletely removed in operations for Graves' disease, the symptoms of myxedema rarely develop; occasionally, however, insufficient thyroid is left and some of the symptoms of cachexia strumipriva may appear.

### (*f*) *Congenital Myxedema*
(*Thyro-aplasia*)

This condition is often wrongly designated sporadic cretinism. Children born with aplasia of the thyroid may look normal at birth and may

do well for four or five months (or until after they have been weaned). Apparently the fetus *in utero* or the suckling infant may receive enough thyroid substance from the maternal organism for the body needs, even when it has no thyroid gland of its own.

A few months after birth, however, severe symptoms rapidly develop. The child becomes abnormally *sleepy,* swallows badly, the body grows *fat* and *plump,* the *skin* of the forehead and elsewhere is thrown up into folds, the *nose* is broad and thick, the nostrils stand wide open, the *eyes* look sunken in the head, the *tongue* is larger than normal, the *mouth* is kept open most of the time, the *lips* are cyanotic and the child drools. The *facial expression* may be that of an old and careworn person. The *hair* is thin, lacks luster, and may grow low down upon the forehead. The skin may have a bluish tint.

As the child grows older the *head* may increase in size, but the rest of the *bony skeleton* remains dwarfed; at the same time the *soft parts* increase in size; a short, thick lump of a child results. Many of the *ossification centers* fail to develop. In the following table, compiled by Dieterle, the time of appearance of the various ossification centers of the bones of the wrist are given. In x-ray pictures of the myxodematous hand, one can decide whether or not we are dealing with a *congenital myxedema* (thyro-aplasia), or an *infantile idiopathic myxedema,* and the exact time of onset of the latter.

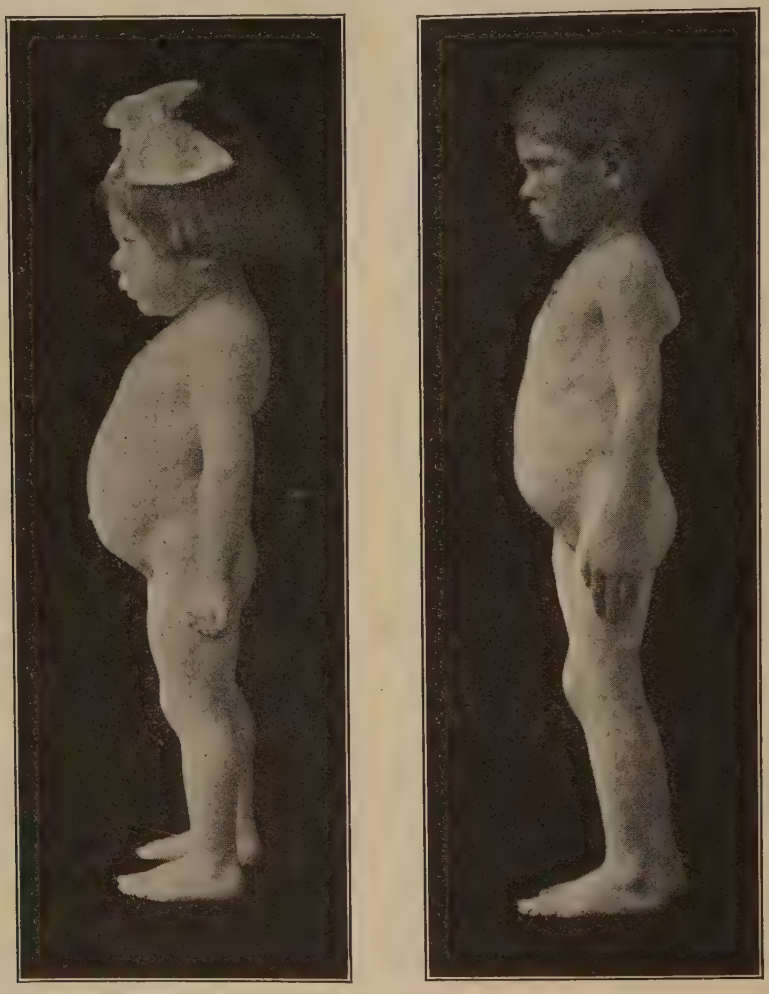
DIETERLE'S TABLE OF THE NORMAL APPEARANCE OF THE OSSIFICATION CENTERS

| Age | Appearance of Bony Shadow | Body Height |
|---|---|---|
| Newborn..... | Diaphysis of phalanges, of metacarpus, of radius, and of ulna.. | 50 cm. |
| 4–8 mo..... | Os capitatum; os hematum..... | 60 cm. |
| 1–2 yrs..... | Epiphysis of radius..... | 75 cm. |
| 2½ yrs..... | Basal epiphyses of proximal phalanges..... | 85 cm. |
| 2¾ yrs..... | Basal epiphyses of terminal phalanges..... | 95 cm. |
| 3 yrs..... | Other basal epiphyses..... | 100 cm. |
| 4–5 yrs..... | Os lunatum..... | 108 cm. |
| 5½–7 yrs.... | Os multangulum majus and minus; os naviculare; distal ulnar epiphyses..... | 110–117 cm. |
| 10 yrs..... | Os pisiforme..... | 135 cm. |
| 13 yrs..... | Sesamoid bones; hamulus ossis lunati..... | 150 cm. |
| 16–17 yrs.... | Disappearance of epiphyseal lines of fingers and metacarpal bones..... | 165 cm. |
| 20 yrs..... | Disappearance of all epiphyseal lines..... | 170–180 cm. |

The *fontanelles* may not close until very late (15th year). The *teeth* come late. The child at puberty may have only one or two molars, and even they may not fully emerge from the gum.

The bowels are usually markedly *constipated* and the abdomen *tympanitic.* Some of the children are distinctly *pot-bellied* or frog-bellied, and many of them suffer from *umbilical hernia. Prolapse of the rectum* is not uncommon.

The children are *anemic* and are *mentally retarded.* The apathy may be so marked that it is difficult to decide at first whether the patients are both deaf and dumb, or only dumb. The children do not learn to walk,



(*a*) (*b*)

Fig. 655.—Myxedematous Girl Before and After Treatment with Kendall's Alpha Constituent of the Thyroid Gland. Eight Months Elapsed Between the Two Pictures, (*a*) and (*b*). The Child Grew Four Inches and Her General Appearance and Mentality Markedly Improved. (By Courtesy of Dr. E. C. Kendall of the Mayo Clinic.)

though they may creep. As a rule they lie all day in bed heavily covered on account of the cold, the fingers in the mouth, exhibiting little or no interest in the surroundings.

Nearly all the cases described in the literature as sporadic cretinism are to be regarded not as cases of true cretinism at all, but as instances of thyro-aplasia, and congenital myxedema. Along with the absence of the thyroid gland, other developmental anomalies may occur (heart, palate, etc.).

In children in whom the symptoms of myxedema do not occur before the third or fourth year, we do not deal with congenital myxedema (thyro-aplasia), but rather with infantile idiopathic myxedema due to some postnatal disease of the thyroid gland.

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### (*g*) *Diagnosis of the Myxedematous States and of Hypothyroidism*

Easy as the diagnosis is in the *typical cases* of **idiopathic myxedema,** much difficulty may be experienced in *atypical cases.*

*Scleroderma* and the edema of *nephritis* are easy to rule out. There may be more difficulty in distinguishing true myxedema from fugacious edemas at the menopause (*ovarian pseudomyxedema*), and in syphilis (*syphilitic pseudomyxedema*). Whether or not the family *trophœdème* of Meige or the *idiopathic edema* of Staehelin are related to myxedema is not clear.

Some cases of *hypophyseal tumor* may closely suggest myxedema, but attention to the hypophyseal signs (headaches, limitation of visual fields, dystrophia adiposogenitalis, x-ray of sella) will suffice to differentiate.

The different forms of *obesity* can also, as a rule, be readily excluded; for in myxedema the hands are greatly thickened, whereas, in obesity, except in the thyrogenous form, the hands and feet usually remain thin. The appearance of the face in obesity differs from that of true myxedema. Though there may be thyroid insufficiency in some of the endogenous obesities, it is usually of a far lower grade than that required for the development of myxedema.

**Congenital myxedema** (*thyro-aplasia*) must be differentiated clinically (1) from *chondrodystrophia* (micromelia, normal intelligence, x-ray of ossification centers; premature ossification of epiphyseal lines); (2) from *genuine cretinism* (endemic occurrence, presence of thyroid gland, often goitrous, skin not myxedematous, sweats often present, heredity); (3) from *Mongolism* (oblique eye-slits, microcephalic skull, red cheeks, comical appearance, small tongue, fontanelle closed before the 4th year, height normal, absence of myxedema in the skin; thyroid feeding fails to benefit the psyche, the facial expression, the joint relaxations or the obesity, but may help the constipation, the umbilical hernia and the meteorism); (4) from *rickets* (softening of bones from poverty of lime and osteoporosis,

swollen epiphyses, bone development not markedly retarded, no delay in ossification at the epiphyseal lines).

The greatest difficulty of all may be experienced in the diagnosis of the *forme fruste* of myxedema or Kocher's **thyropenia**. It may be suspected in children of *backward growth,* in children who are *dull at school,* and in both children and adults who are *habitually constipated* without apparent cause. It should also be thought of in the *endogenous obesities* and in women who present *neurasthenic* symptoms suggesting premature menopause. When latent, a thyropenia may manifest itself during pregnancy, or after a severe hemorrhage, or as old age approaches, though by no means all cases of marasmus senilis are attributable to thyropenia.

The *therapeutic test* may be useful in diagnosis. Thus, in adults, tablets of dried thyroid substance, and in children, fluid thyroid elixir may be tried. If the symptoms are due to deficiency of the thyroid function, favorable results follow promptly. The swelling of the skin diminishes, the patients feel warm again, the apathy disappears, and mental alertness and bodily liveliness return. The hair stops falling out, the amenorrhea disappears, and the metabolism becomes accelerated. These changes will appear within a month if two to four tablets be given per day, and the symptoms will reappear again by the end of three months if the therapy be stopped. Once the symptoms have disappeared, it is surprising what small quantities of thyroid substance, continuously administered, will suffice to prevent the reappearance of symptoms. In true endemic cretinism, on the other hand, thyroid tablets as a rule do not benefit; in many instances symptoms of thyro-intoxication appear (emaciation, diarrhea, tachycardia, sweats).

Kocher has tabulated a comparison of the symptoms in myxedema and in Graves' disease, as follows:

| MYXEDEMA. | GRAVES' DISEASE. |
|---|---|
| 1. Absence or atrophy of thyroid gland. | 1. Enlargement of thyroid, usually diffuse; increased vascularity. |
| 2. Slow, small, regular pulse. | 2. Frequent accelerated pulse, often irregular. |
| 3. Vasomotors negative. | 3. Very excitable vasomotors. |
| 4. Apathetic, quiet look; expressionless. | 4. Anxious look; on fixation of eyes, suggestion of anger in facial appearance. |
| 5. Narrow lid-slits. | 5. Wide lid-slits; protrusio bulborum. |
| 6. Slow digestion and excretion; anorexia. | 6. Abundant excretions; appetite usually abnormally great. |
| 7. Slowed metabolism. | 7. Accelerated metabolism. |
| 8. Thick, non-transparent, wrinkled, dry and desquamating skin. | 8. Thin, transparent, vascular, moist skin. |
| 9. Short, thick fingers, often broad at the ends. | 9. Long, slender fingers with tapering terminal phalanges. |

| MYXEDEMA. | GRAVES' DISEASE. |
|---|---|
| 10. Drowsiness and sound sleep. | 10. Insomnia and restless sleep. |
| 11. Dulled sensation, apperception and action. | 11. Hypersensitiveness; lively apperception and action. |
| 12. Poverty of thought; apathy; lack of feeling. | 12. Flight of ideas; mental excitations; sometimes hallucinations, mania or melancholia. |
| 13. Clumsiness. | 13. Restless haste. |
| 14. Stiffness of the extremities. | 14. Tremor of the extremities; increased mobility of joints. |
| 15. Retardation of bony growth; bones short, thick or deformed. | 15. Delicate bony structure; now and then soft, thin bones. |
| 16. Constant feeling of cold. | 16. Unbearable feelings of heat. |
| 17. Slow, deep breathing. | 17. Superficial breathing with faulty inspiratory expansion of thorax; often tachypnea. |
| 18. Increase of body weight; obesity. | 18. Loss of weight; emaciation. |
| 19. Senile appearance, even in young. | 19. Youthful appearance, especially at the beginning. |

## 4. Cretinism

### (*a*) *Conception of the Disease*

For the reasons mentioned under myxedema, we do not regard so-called sporadic cretinism as true cretinism. We may define *true cretinism* as an endemic disease, associated with certain special regions of the earth, and characterized by certain physical signs (thyroid, bones, skin, genitals), mental changes (feeble-mindedness, indolence), and defects in the organs of special sense (deafness, etc.).

### (*b*) *Geographical Distribution of Cretinism*

Cretinism, in the sense defined above, is a widespread disease, occurring in many different countries, where its prevalence is a matter of great social significance for the peoples of those countries. The cases are relatively most numerous in Switzerland, in certain valleys of which nearly all the population are more or less affected. The criminal rate and the insane rate are said to be very high in Switzerland; some assert that this is largely owing to the prevalence of cretinism. In certain parts of Austria (Steiermark), and of Italy (Piedmont, Lombardy, Venetia), there are a great many cretins. The general distribution in Europe is well shown in the map in Vogt's article (See references).

In America but little has been written about true cretinism. We see cases among immigrants, but most of the cases referred to in the bibliography as cretins are instances of myxedema.

### (c) *Forms of Cretinism*

It is customary to group together (1) *endemic cretinism* in its outspoken form, which is the so-called *typical cretinism,* and (2) certain *partial forms of cretinism,* including (a) *endemic goiter,* (b) *endemic deaf-mutism,* and (c) *endemic strumous imbecility.* The symptoms of typical endemic cretinism will first be described, and subsequently those of the partial forms will be taken up.

#### i. Symptoms of Typical Cretinism

Every traveller through Switzerland must have become familiar with the appearance of the typical cretin. The *prognathic face,* as broad or broader than its length, is characteristic, with its low forehead, broad nose and deep grooves. The nostrils project forward, the malar bones are prominent, and the mouth looks large. The *tongue* is large and juicy, the *lips* thick. The *body* is short and looks especially small when contrasted with the large *quadrangular head.*

The patients are *flat-chested* and often *pot-bellied.* The upper and lower *extremities* are short and plump, as are the fingers and toes. Those affected *walk* slowly with a broad base. The movements of cretins, whether of hands or feet, are slow and clumsy.

The *skeletal changes* have been carefully studied. Ossification is retarded and the growth in length of the bones is markedly interfered with.

The *skin* shows peculiar changes. It is thick and loose, looks wrinkled and faded, and may be pale white in color or slightly yellowish in tint. The *hair* is scanty, dry, breaks easily, and tends to fall out. The *nails* are dry and fragile. The *subcutaneous tissue* may be thickened in various regions, especially on the neck and on the backs of the hands and the feet. The visible *mucous membranes* may also be relaxed and thrown up into folds. Through all these changes the patients look older than their years.

While a few cretins are developed sexually, in the majority the *external genitals* remain infantile. Many of the girls never menstruate. Occasionally a cretin bears children, when the disease is mild, but the children are usually still-born, or die soon after birth, and, frequently, they show malformations. The *secondary sexual characters* are often lacking; the crines pubis and the hirci are scanty; the breasts remain small, the voice continues infantile.

Many of the patients suffer from *colloid goiter,* though some have thyroid glands of normal size. According to Ewald, 63 per cent of all cretins suffer from struma.

The *metabolic processes* are slowed. Obstinate constipation is a common symptom.

The *psychic manifestations* are very important. The majority of outspoken cases are mentally deficient. One sees every grade, from outspoken idiocy, through imbecility, to slight debility. The majority are apathetic, dull and indolent; indeed, the slowing of all the mental reactions and the slow, clumsy movements are very characteristic of the disease. Some cretins are able to do a little work. In Switzerland, cretins are utilized for various lowly duties requiring little or no head-work. Many of them become beggars. Fortunately the great apathy in the majority of the severer forms diminishes criminality, but in the less severe forms and in some outspoken cretins there is extraordinary irritability, and in such instances violent outbreaks are not uncommon.

Disturbances of hearing (*deafness*), and of the other special senses, are very common. Though without discriminating taste, many cretins are *gluttons*. The *pain sense* seems dulled, though no complete anesthesia for any modality of sensation in the skin is found.

In regions in which these outspoken or typical cases described above are met with, there also occur large numbers with the partial manifestations to be mentioned below.

### ii. Symptoms of Partial Cretinism

**Endemic Goiter.**—The pedestrian in the valleys of Switzerland and of the Tyrol will remember the large number of deforming goiters met with in a day's tramp. The whole gland may be affected, or only a part of it. The right lobe is more often involved than the left. The volume of the goiter varies from time to time. The *mechanical effects* of the goiter may be serious (venous obstruction, dyspnea, tachycardia, dysphagia). Many typical cretins suffer from goiter, but in the same regions, there are many people who have goiter who do not present the other symptoms of cretinism. Between these two groups are many patients who have goiter and who present *mild signs* of cretinistic degeneration (mental dullness, clumsy behavior, laziness, etc.). The latter have been designated by Weygandt as cases of *endemic strumous feeble-mindedness*. In other instances, the feeble-mindedness may occur without struma, the only other signs being small stature or mild cutaneous manifestations.

**Endemic Cretinistic Deaf-mutism.**—Deaf-mutism is very common in cretinistic regions; thus, in the Province of Steiermark alone, there are over 2,000 deaf-mutes, and in Switzerland, the percentage of deaf-mutes among the population exceeds that of any other civilized country. The deafness appears to be due to a direct injury to the labyrinth, probably an involvement of the growth of the bones during the development of the base of the skull. About 50 per cent of these deaf-mutes have goiter, but the labyrinthine change appears to be independent of the thyroid injury.

### (*d*) *Anatomical Changes in Cretinism*

The changes in the bones, the *cretinoid dysplasia* of Klebs, depend upon alterations in the cartilage cells. Both long and short bones are affected. Ossification is retarded; this is proven, not only by autopsies, but by x-ray examinations made during life. The internal organs and the muscles are small, and the sexual organs are infantile. Various alterations in the nervous system have been described, but nothing specific or constant has been found.

### (*e*) *Etiology and Pathogenesis of Cretinism*

The cause of cretinism is unknown, though its endemic distribution makes it seem certain that either the *water* or the *soil* is *responsible.* According to Bircher, certain *geological formations* in Switzerland (Trias, Meermolasse, Eocän) are responsible, while regions with other formations (Lava, sediments of the Jura and of the Chalk Sea, of the Quaternary Sea and all fresh water deposits) are free from cretinism. It must be admitted that the maps showing the distribution of cretinism accord very well with this view.

What the *exogenous factor* is that is derived from the water or soil we do not know. It is certain that persons who come into cretinistic regions from the outside often develop goiter. Many of the inhabitants forbid water drinking, even the children being required to drink wine. In an acute outbreak of goiter in Nancy, it is asserted that army officers who drank wine were not affected. Dogs and rats drinking the "goiter water" develop struma. Most believe that the noxa is an organic substance, some assuming the existence of a specific microörganism; others blame some organic chemical substance, though there are also adherents of the view that mineral constituents (Mg, S, Ca) are responsible. The tendency of the Swiss and Austrian investigators is to regard the disease as a water-borne *infection,* the germ being harbored by certain marine deposits on the earth's crust.

Formerly it was thought that the noxa caused injury wholly through its action upon the thyroid gland. Undoubtedly, the thyroid is diseased in the majority of cretins, though perhaps not in all, and doubtless, the hypothyroidism occurring in early life is an important factor in the growth disturbances and other alterations of the disease; but the thyropathy will not account for the whole clinical picture. The total pathogenesis of cretinism is as yet far from clear.

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# C. Diseases of the Parathyroid Glands

*(The Parathyropathies)*

Concerning no other gland of internal secretion are we as well informed regarding the signs that follow *total removal* and *insufficient function* as in the case of the parathyroids. Concerning *over-activity* of the parathyroid gland, we know as yet little or nothing, though many hypotheses have been advanced.

## 1. States Due to Loss of Function or to Insufficiency of Function of the Parathyroid Glands

*(Tetany and Tetanoid States)*

### (*a*) *Conception of Tetany*

Tetany is a clinical syndrome due to insufficient function of the parathyroid glands, characterized in its outspoken form by (1) paroxysmal *tonic contractions,* often painful, usually confined to certain definite groups of muscles, and unaccompanied, as a rule, by loss of consciousness; (2) *paresthesias* in the extremities; (3) certain *trophic disturbances* (hair, teeth, nails, lens); and (4) *certain signs* that can be experimentally elicited, dependent upon over-excitability of the nerves, including (a)

the *Trousseau phenomenon*, (b) the *Chvostek phenomenon*, and (c) *Erb's sign*.

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### (*b*) *Historical Notes Concerning Tetany*

Some of the symptoms of tetany were described in 1830 by Steinheim and in 1831 by Dance. About the middle of the last century, the disease occurred in epidemic form in Paris and stimulated the important studies of Corvisart and of Trousseau. The former introduced the name *tetany* in 1852 and the latter studied

the disease in 1851, and, nine years later, discovered the possibility of artificially producing the typical contracture-position of the hand by placing a ligature on the upper arm, even when the disease was latent.

Viennese physicians, later, made important contributions. Thus, in Billroth's clinic, in 1880, the occurrence of tetany after removal of the whole thyroid for goiter was observed and reported (Weiss). This observation stimulated much experimental work on animals in various countries (Schiff, Sir Victor Horsley, von Eiselsberg, W. S. Halsted, T. Kocher). The discovery that the parathyroid glands are anatomically independent of the thyroid gland (Sandström, Gley,

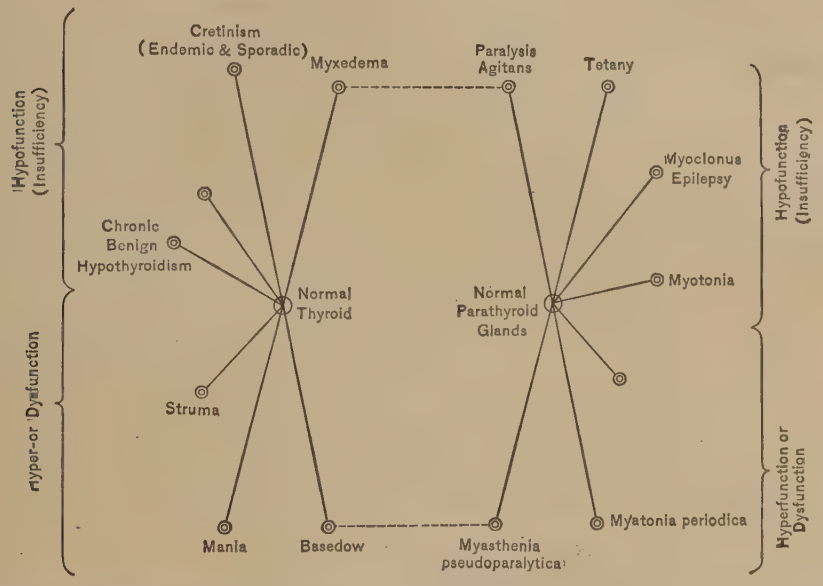


**Fig. 656.—Possible Relations of Thyroid and Parathyroid Glands to Different Disease Conditions. (After A. Biedl, "Innere Sekretion," published by Urban & Schwarzenberg, Berlin.)**

Kohn), and the investigations of the physiological functions of the parathyroids (Vassale and Generali, 1896) soon showed that the tetany following thyroidectomy is due, not to the loss of the thyroid-function, but to the loss of function of the parathyroid glands simultaneously removed.

The identity of *experimental tetany* in animals with *human tetany,* and the recognition that all the various forms of tetany clinically described have a common basis in *parathyroid insufficiency,* followed from a long series of experimental and clinical observations (Jeandelize, 1902; Pineles, 1904–1907; Erdheim, 1901–1911; von Fraenkel-Hochwart; W. G. MacCallum; C. Voegtlin).

As a crown to the edifice, thus laboriously constructed, came the astounding discovery that, in cases of parathyroid insufficiency, living parathyroid glands can be *transplanted,* and will grow and functionate, at least for a number of years, thus completely curing the tetany. The animal experiments of Cristiani and others brought proof of this. Leischner suggested its practical significance in the treatment of human disease, and von Eiselsberg first successfully transplanted the human parathyroid to cure tetany. At least nine human transplantations have been reported; in three, the tetany was cured; in three more, the symptoms were

markedly lessened; in two of the cases, no benefit followed. In the United States, W. S. Halsted and C. H. Mayo have contributed to our knowledge of the surgery of the parathyroids.

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### (c) Symptoms of Tetany

These consist of (1) certain peculiar tonic contractions of the voluntary muscles, (2) certain subjective and objective sensory disturbances, (3) vasomotor, trophic and secretory disturbances, (4) the so-called latent symptoms, and (5) certain other symptoms.

#### i. The Tonic Contractions of Tetany

In attacks of tetany, *tonic spasm* occurs in certain muscles, especially in the *upper extremities,* resulting in a characteristic position of the hand

(*obstetrical hand*). The proximal phalanges are flexed, while the middle and distal phalanges are extended. The thumb is turned into the palm and firmly held against the other fingers. The wrist is only slightly bent backward or forward, the elbow is held midway between flexion and extension, with the upper arm adducted.

Similar spasms occur in the *lower extremities* with extension of the hip and knee, and strong plantar flexion of the foot and toes, with supination of the ankle, and adduction of the thighs.

The so-called *carpopedal spasm* of children is a tetanic spasm, involving the distal parts of both upper and lower extremities. This spasm, or at least one that resembles it closely, is sometimes referred to as arthrogryposis. The convulsions of childhood (eclampsia) are often due to tetany.

Spasm of the muscles of the face and trunk are rare, though the *facial expression* is sometimes characteristic (angles of the mouth drawn down, deep nasolabial folds, forehead wrinkled, wide lid-slits). This is known as the "tetany-face" of Uffenheimer. In children, the lips may be protruded and slightly pointed ("carp-mouth)."

The *laryngospasm* of children is nearly always a symptom of tetany. It may also occur in adults. Laryngospasm is not free from danger. After a long noisy inspiration, the respiratory muscles, including the diaphragm, become rigid in the inspiration-position, more rarely in the expiration-position. Death may occur in the attack. Fascicular muscle twitching is not uncommon in the parts subject to spasm in tetany.

The spasm of tetany may be *painful* or may be associated only with a *feeling of tightness* in the parts and *paresthesia*. Though usually bilateral, an attack may be unilateral in distribution. The spasm lasts from a few seconds to several hours or days. In some children, we sometimes observe the contractions of tetany persisting continuously for days or weeks (*tetania persistens*).

In tetany, an attack of the spasm may be brought on by physical or mental shock, or by overuse of the muscles concerned. In addition to the tonic spasms, *clonic contractions* resembling those of eclampsia are occasionally met with. In the tetany following removal of the parathyroids at strumectomy, true *epileptiform seizures* sometimes occur. The attacks differ from ordinary idiopathic epilepsy through the predominance of the tonic contractions in the attack, the non-response to bromid treatment, and the presence of the latent signs of tetany.

### ii. Certain Subjective and Objective Sensory Disturbances in Tetany

Among these, the *paresthesias* of the distal portions of the upper extremities, and the *feelings of tension* in the arms and legs are the more important. Occasionally, objective *anesthesias*, including analgesias, are met with, but they are rare. *Tinnitus aurium* may be present, but hearing, smell and taste are not involved.

### iii. Vasomotor, Trophic and Secretory Disturbances in Tetany

Some patients present pallor of the skin, *dermatographia, angioneurotic edema,* or *erythemas.* The trophic disturbances in the nails, hair and teeth are especially worthy of mention and may often call the attention of the physician to the existence of a chronic or latent tetany. The *nails* may be fragile or transversely ridged. The *hair* often falls out and, in the chronic cases, is usually thin and short. When tetany occurs in childhood, the *enamel* of the teeth does not develop properly; it shows transverse furrows and small holelike defects. The teeth may be marked by several *horizontal grooves* of enamel defect, which make sets of parallel lines running along the teeth. The incisors and canine teeth are most often affected, the molars more rarely (Fleischmann). Similar trophic disturbances occur in the teeth of rats in experimental tetany (Erdheim).

Fig. 657.—Trophic Disturbances (Dystrophy?) of the Teeth in a Case of Chronic Recurrent Tetany with no Traces of Rachitic Bone Changes. (After E. Phelps, in "Handb. d. Neurol.," published by J. Springer, Berlin.)

One of the most interesting trophic disturbances in tetany is a peculiar form of cataract formation (Peters). It is a *perinuclear cataract,* which usually causes no subjective disturbances of vision. To discover the cataract the pupils should be dilated and the examiner's eye helped by a strong plus glass when the turbidity will be discovered in typical perinuclear arrangement. It may be the only sign remaining of an earlier tetany, though, when present, the latent signs of parathyroid insufficiency (see below) may be elicitable. The cataract is usually bilateral.

In the domain of the secretory nerves symptoms are rare, though occasionally *salivation, sweating* or *polyuria* have been met with.

The disturbances in *calcium metabolism* and of the *growth of bones* in tetany, and the relation of tetany to rickets require further study.

### iv. The Latent Signs of Tetany

Between attacks of tetany, and, in some patients, even years after any spontaneous attack has been observed, certain signs peculiar to tetany can be artificially provoked. Among these will be mentioned, (1) Trousseau's phenomenon, (2) Chvostek's phenomenon, and (3) Erb's phenomenon.

**Trousseau's Phenomenon.**—This is certainly one of the most important signs of latent tetany (Trousseau, 1864). If a blood-pressure apparatus be applied to the upper arm, and the pressure in the cuff be raised to a point above that necessary to obliterate the radial pulse (thus avoiding venous stasis), in a short period, varying from a few seconds to a few minutes, the typical *obstetrical-hand attitude* appears.

In mild cases of latent tetany, this may be preceded by fascicular twitching in the small muscles of the hand, especially between the metacarpal bones of the thumb and index finger, and in the muscles of the forearm. Now and then, the

Fig. 658.—Typical Position of the Hand in an Attack of Tetany. This Is the So-called "Obstetrical Hand." The Same Appearance, Due to Pressure Upon the Upper Arm, is Known as Trousseau's Phenomenon. (After E. Phelps, in "Handb. d. Neurol.," published by J. Springer, Berlin.)

typical contracture does not appear and one sees nothing but these fascicular twitchings, the patients complaining of a tight feeling in the arm and hand and of peculiar paresthesias.

The phenomenon is due to the *pressure upon the nerves* in the medial bicipital groove. Instead of the blood-pressure apparatus, one may apply a rubber bandage around the upper arm, inserting, finally, a small roll of the bandage beneath the last turn in the medial bicipital sulcus so as to increase the pressure on the nerve trunks.

Trousseau's phenomenon can be elicited in the majority of cases of tetany, but sometimes it is not demonstrable even when the tetany is pronounced. A negative result, therefore, does not rule out tetany.

Ice and hot water applied to the medial bicipital groove will also elicit Trousseau's phenomenon (Kaschida).

Similar contractures can sometimes be elicited in the lower extremities (H. Schlesinger). If the lower extremity be extended at the knee, and strongly flexed at the hip, a tonic spasm appears in the extensors of the leg and supinators of the foot, usually within a couple of minutes.

**Chvostek's Phenomenon.**—This depends upon increased mechanical excitability of the motor nerves in tetany (Chvostek, Sr., 1878). Thus, if

the trunk of the facial nerve, in front of the ear, be tapped with a percussion hammer, a quick contraction of the facial muscles follows (*facial phenomenon*). Sometimes a contraction is obtained on tapping a spot just below the anterior part of the zygoma. The contraction is usually most easily seen at the angle of the mouth.

*Three degrees* of the facial phenomenon are distinguished by von Fraenkl-Hochwart, as follows:

Chvostek I. Contraction in the whole domain of facial innervation on tapping the trunk of the facial.

Chvostek II. Contraction at the ala nasi and angle of the mouth on percussion below the zygoma.

Chvostek III. Contraction at the angle of the mouth only on tapping the zygoma.

This facial phenomenon may occur in conditions other than tetany, though Chvostek I is rare except in tetany. The lesser degrees of it have been met with in incipient pulmonary tuberculosis, in neurasthenia, in epilepsy, and, occasionally, in apparently healthy persons. Undoubted cases of tetany have been observed in which Chvostek's sign could never be elicited. On the other hand, this facial phenomenon is often present as a latent sign when other signs have disappeared.

The *direct mechanical excitability of muscles* seems also to be increased in tetany. This accounts for the *tongue phenomenon* of Schultze, a depression appearing in the tongue if it be tapped. If a spot on each side of the tongue be tapped in quick succession, the contraction leads to a constriction of the whole tongue opposite the two points tapped.

**Erb's Phenomenon.**—This sign depends upon the *increased electrical excitability of the motor nerves* in tetany (Erb, 1878). To demonstrate its presence, it is necessary to determine, in each case, the threshold values on electrical stimulation and to compare them with the normal values in Stintzing's tables, keeping in mind the fact that the variations within normal limits are considerable. In addition to the lowered threshold, certain changes in the contraction-formula are characteristic of tetany; thus, even if the cathodal-closure contractions show normal values, (1) an early appearance of a cathodal-closure tetany, (2) an early appearance of an anodal-closure contraction followed quickly by an anodal-opening contraction, and, especially, (3) the appearance of a cathodal-opening contraction, indicate a heightened electrical excitability.

The test is best carried out on the *N. ulnaris*, which innervates the muscles usually attacked by the spasm of tetany, but other nerves should also be examined on both sides of the body. One should not be satisfied with a single examination, but should make tests on successive days, and especially, should opportunity arise, just after an attack (Stewart).

In some cases, the electrical excitability increases during the examination (*excitation-reaction* of Bechterew).

Erb's sign is especially valuable in the studies of *tetany in children,* being, according to Escherich, more constant in them than either the Trousseau phenomenon or the Chvostek phenomenon. In children, it is best to test the *N. peroneus* at the head of the fibula. The normal threshold in children is higher than in adults. For a careful study of the condition in children, the reports of von Pirquet should be consulted.

Aside from the above galvanic tests, it has been shown by Chvostek, Jr., that *faradic stimulation of nerves* in tetany often calls forth a fibrillary wavelike contraction in the muscle, to be followed quickly by tetanic contraction (facial nerve, ulnar nerve).

### v. Other Signs of Tetany

The *sensory nerves* are also over-excitable in tetany (Hoffmann). Thus, tapping the supra-orbital nerve causes pain and paresthesia and the *electrical-stimulus-threshold* is low. The latter is true also for the acoustic nerve, a galvanic current of 2.5 milliampères causing, on cathodal closure, a distinct sound in the ear.

The *reflexes* in tetany show no constant alterations; they may be slightly increased, they may be diminished, or they may be absent. The voluntary muscles *fatigue* easily on exertion. In some instances, the pelvic and lumbar muscles are especially weak, the weakness giving rise to a peculiar *waddling gait,* suggesting progressive muscular dystrophy. Occasionally, actual *pareses* and *atrophies* of muscle have been observed.

Certain *asthmatic attacks* seem to be due to tetanic spasm of the diaphragm. The *body temperature* is usually normal, though, sometimes, slight remittent fever is present. Some patients show a subnormal temperature.

In both acute and chronic tetany, *disturbed mental states* are common. In the acute forms, irritability, mental apprehension, and anxiety states are not infrequent. In the chronic forms, the patients may present general *neurasthenic symptoms,* or even signs that make one suspect *mental deterioration* (injured recording faculty; feeble memory; lack of concentration).

Outspoken *psychoses* are rare, but they may occur. They may take the form of hallucinatory confusion (von Fraenkl-Hochwart). The rigidity of catatonic states must not be confused with the cramps of tetany.

## (*d*) *The Etiology and Pathogenesis of Tetany*

The disease is especially prevalent during *certain months* of the year; thus, January, February and March are often spoken of as tetany months. Tetany occurs in *epidemics* during these months.

The *endemic* character of tetany is also well established. In *certain cities* like Vienna, Paris and Heidelberg the disease is especially prevalent, while many cities remain almost free from the disease.

Several members of one *family* may be simultaneously affected. Whether this depends upon heredity or upon environmental conditions is not certain. Since several generations in the one family have been known to suffer from the disease, it seems probable that in some cases *inheritance* is important. *Males* are more often attacked than females. Men engaged in certain special *occupations* (shoemakers, tailors, metal workers) seem peculiarly liable to the disease. Crowded quarters and *bad hygienic surroundings* certainly predispose.

The *tetany of childhood* is most common in the second half of the first year of life. It rarely appears for the first time before the third month, or after the third year (Potpeschnigg). Another period of life in which tetany is common is *late adolescence* (17th to 20th year). In later life, tetany is sometimes associated with (1) *maternity,* (2) *gastro-intestinal diseases,* (3) *infections and intoxications,* and (4) *strumectomy.*

The tetany of young adults is often described as *idiopathic tetany.* It begins as a rule with paresthesias in the distal parts of the extremities, and these are followed later by the typical cramps in the arms or legs. Some of the patients affected give a history of tetany in early childhood; in a few of them, the residues of an earlier tetany are visible in the form of perinuclear cataract or of the tetany teeth.

The so-called *maternity tetany* may occur at any period of pregnancy or lactation, but, like all forms of tetany, it is most common in the so-called tetany months. Some women suffer from tetany every time they have a child. In chronic tetany, uterine contractions may set up the tetanic spasms (Gross). Epileptiform convulsions sometimes accompany maternity tetany.

Maternity tetany has been observed in animals. In a bitch, operated upon by Halsted, from which half the thyroid had been removed, pregnancy occurred later and was accompanied by pronounced tetany shortly before the birth of the litter. In an animal operated upon by Vassale, the partial parathyroidectomy was followed by typical tetany, during lactation, after two successive pregnancies. Similar phenomena have been observed in rats by Erdheim and his pupils.

It seems obvious that in pregnancy and lactation greater demands are made upon the parathyroid functions than at other times. Whether this is related to the hypertrophy of the adrenals, which are believed to be antagonistic to the parathyroid bodies, is not yet certain.

The *tetany accompanying gastric dilatation* long since attracted the interest of clinicians. Other disturbances of the digestive organs (cholelithiasis, pyloric stenosis, carcinoma ventriculi, helminthiasis) have been accompanied also by tetany, sometimes in mild form, sometimes of the more severe and chronic types.

In the case of gastroduodenal dilatation studied by Estes and myself, spasms resembling those of tetany occurred.

Tetany is an occasional *complication* of typhoid fever, influenza, pneumonia, tonsillitis and other infectious diseases. It is also occasionally observed in various intoxications (saturnism, ergotism, alcoholism, morphinism, etc.).

The *tetany following strumectomy* is of great historical interest, since it was the

studies of this form that led to the experimental investigations that made clear its relation to parathyroid insufficiency. Such postoperative tetanies may set in within twenty-four hours after the operation, or at any time during several weeks thereafter. The spasms are usually severe and sometimes have a fatal termination, especially when laryngospasm occurs. Epileptiform convulsions are frequent in this form of tetany. The latent signs of tetany can be elicited. Psychic disturbances are common and trophic changes in the nails, hair, teeth and lens may develop.

Outspoken tetany following strumectomy (*tetania thyropriva*) has become very uncommon, since surgeons have learned how to remove a goiter without at the same time excising the parathyroids. Still, one or more parathyroids are often removed or injured at the operation, or the parathyroids left may become involved in inflammatory processes, with resulting parathyroid insufficiency. Accordingly, mild forms of tetany are still not infrequently met with in surgical practice. Most of the patients recover, though they may later on have recurrences, especially in the tetany months.

The **unity of all forms of tetany** postulated by Schultze (1895), and Pineles (1906), depending upon the common factor of parathyroid insufficiency, ought, it seems to me, to meet with general acceptance by clinicians. The clinical and experimental evidence in favor of this view is now overwhelmingly convincing.

The four parathyroid glands are not always equal in size or equivalent in function. One of these glands may apparently always be removed without injury, provided the others are functioning normally. In the forms of tetany independent of thyroidectomy, a *functional insufficiency* of the parathyroids probably exists.

Post-mortem examinations of parathyroid glands have shown that hemorrhages, inflammations, cysts and neoplasms occur in them, but, strange to say, tetany has not been common in association with the cases that have been studied pathologically. In cases of tetany studied post mortem, positive **pathological findings** in the parathyroids have been met with in many cases, but in just as many other cases no anatomical lesions of the parathyroids were found. We must assume for the present that functional insufficiencies can be responsible for tetany in the absence of demonstrable anatomical lesions.

*Just why and just how the body suffers in parathyroid insufficiency* is not yet clear, though **metabolic studies** in experimental animals have already yielded certain clues that may prove to be important. The *diminished carbohydrate tolerance,* the *increased calcium excretion* (MacCallum and Voegtlin), the *increased excretion of chlorids,* the *eosinopenia,* and the *increased ammonia-content* of the blood (Carlsen and Jacobson) may be mentioned in this connection. MacCallum suggests that the increased excitability of the nervous system may be related to the loss of calcium. Some of the symptoms may depend upon the interference with the general balance of the endocrine organs that results from the parathyroid insufficiency; thus, there is some evidence that over-activity of the chromaffin-system and of the thyroid gland accompany tetany.

Some authors regard the parathyroid secretion as *antitoxic* in function; others think, rather, that the glands produce one or more *hormones* that are important for the function of the rest of the body.

The *similarity of tetany to convulsive ergotism* has been emphasized by A.

Fuchs. Signs of tetany were produced in men with intestinal disturbance by Eppinger on administration of 5.0 g. of histidin hydrochlorate. Biedl suggests that the β-imidazolylethylamin of Barger and Dale is the most active substance of ergot and may also be the tetany poison. There are many objections, however, to identifying the phenomena of ergotism with those of tetany.

The **hormone-doctrine of tetany** seems steadily to gain adherents, and evidence favors the view that the hormone acts chiefly upon certain higher reflex neurons in the central nervous system (Horsley, MacCallum). The clinical symptoms of tetany point to an action upon the neurons of the medulla oblongata (innervation of respiration and circulation, glycosuria, polyuria), and upon the cervical and lumbar enlargements of the spinal cord (bilateral tonic spasm, fascicular twitchings, paresthesias).

### (*e*) *The Prognosis in Tetany*

This should be *guarded,* especially in postoperative cases, for these not infrequently terminate fatally. The majority of cases of all forms of tetany recover, though the possibility of recurrences in the tetany months, at different periods of life, must be kept in mind. The great frequency of *latent tetany* is at present largely overlooked by practicing physicians. The importance of keeping chronic tetany in mind in patients presenting psychoneurotic symptoms is well shown by the case recognized and reported by J. P. Munroe of Charlotte, N. C. The tetany of childhood may not be followed in later life by any other signs, though sometimes trophic residues (*vide supra*) are observable, and not infrequently, in later life, acute or chronic tetany occurs.

### (*f*) *The Diagnosis of Tetany*

The diagnosis of tetany is easy in the cases with typical tonic spasms without loss of consciousness. The demonstration of the latency-signs corroborates the diagnosis. Tetany would be less often overlooked if certain predisposing factors (pregnancy, gastro-intestinal diseases, strumectomies, specific occupations, time of year) were not lost sight of.

A positive diagnosis does not require the demonstration of all three main latency-signs; any one may be absent. The finding of *trophic residues* of childhood tetany may be helpful.

It may be necessary to differentiate tetany (1) from *epilepsy,* (2) from *hysteria,* (3) from *catatonia,* (4) from *tetanus,* and (5) from *cramps in muscles due to other causes.*

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# D. Diseases of the Hypophysis Cerebri or Pituitary Gland (The Hypophysopathies)

## 1. The Structure of the Hypophysis Cerebri

The hypophysis cerebri consists of an anterior glandular part (*lobus anterior*) and a posterior nervous part (*lobus posterior* or *pars nervosa*), closely connected with which is the so-called *pars intermedia*. Each of these three divisions of the gland possesses special functions.

The hypophysis lies in the *sella turcica* of the base of the skull. The posterior lobe is connected directly, through the infundibulum, with the brain; a small process of the anterior lobe runs up into the pedicle of the hypophysis.

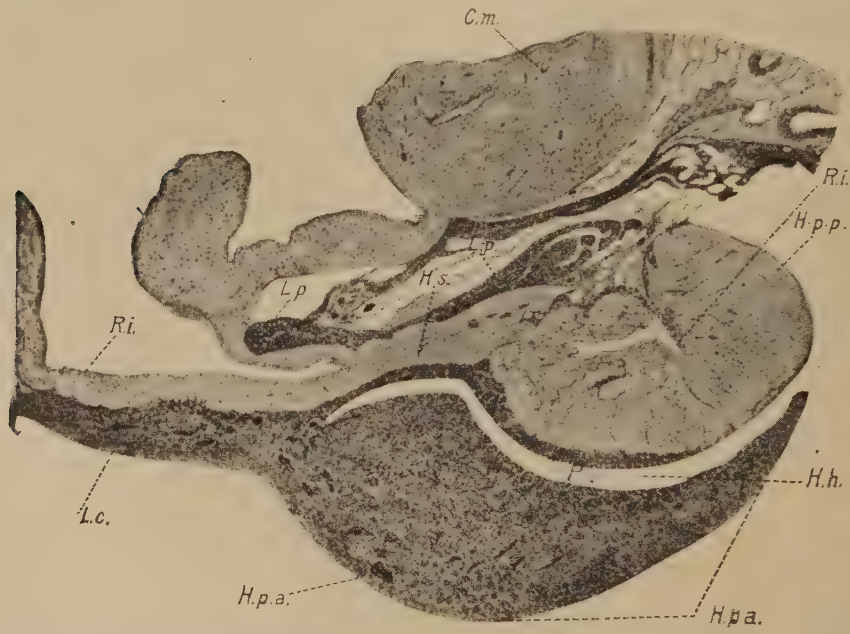


Fig. 659.—Sagittal Section Through the Hypophysis of a Cat. C.m. = Corpus mam.; H.p.a. = Ant. Lobe of Hypophysis; H.p.p. = Post. Lobe of Hypophysis; H.s. = Hypophyseal Stalk; R.i. = Recessus infundibularis; P.i. = Pars intermedius; L.c. = Lobulus chiasmaticus; L.p. = Lobulus premammillaris. (After A. Biedl, "Innere Sekretion," published by Urban & Schwarzenberg, Berlin.)

The **anterior lobe, or pars glandularis,** consists chiefly of epithelial columns lined by the so-called chief cells (*chromophobe* or *neutrophilic cells*). Toward the posterior part of the anterior lobe are situated certain *chromophile cells* that are subdivisible, by special staining methods, into (1) *eosinophilic* or *acidophilic cells*, and (2) *cyanophilic* or *basophilic cells*. In the same region lies the so-called *Rathke's cyst*.

Embryologically, the anterior lobe is derived from the mouth cavity at its junction with the head gut.

The **posterior lobe,** including the pars nervosa or neurohypophysis and its epithelial envelopment (the pars intermedia of Herring), is embryologically derived from the nervous system. The pars nervosa is made up, histologically, chiefly of neuroglia. The origin of the substance upon which the physiological activity of this portion of the gland depends is not clear. The pars intermedia is a thin epithelial covering, thickest at the anterior part of the pedicle, where the pars intermedia joins the anterior lobe.

The lobus anterior is very vascular and apparently secretes a *stainable colloidal substance* as an internal secretion that passes into the blood. The relatively non-vascular pars nervosa contains in its meshes *colloidal or hyaline masses* that may represent an internal secretion that is discharged into the cerebrospinal fluid (Cushing and Goetsch). It has been hinted that this colloidal substance found in the pars nervosa may be a secretion from the cells of the pars intermedia. The *parahypophysis* (Dandy and Goetsch), present in the floor of the sella turcica in cats and dogs, has not been described in man.

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## 2. The Functions of the Hypophysis Cerebri

As with the thyroid gland, diseases of the hypophysis are accompanied sometimes by symptoms that appear to be due to *over-function* of the gland (*hyperhypophysism*), sometimes by symptoms due to *under-function* (*hypohypophysism*). In many cases, however, the function is so perverted (*dyshypophysism*) that symp-

toms usually attributed to over-function may be combined with symptoms usually attributed to under-function. It may be that in every case of hypophyseal disease we deal with such a dyshypophysism or dyspituitarism; but for clinical analysis, it will be easiest if we consider, first, the states due predominantly to over-function and afterward the states due predominantly to under-function.

Since P. Marie (1886) described acromegaly, and later, with Marinesco, showed that the disease is due to a pathological change in the hypophysis, the functions of this body have been the subject of much physiological experimentation.

Intravenous injections of *extracts of the whole gland* raise the blood pressure (Oliver and Schäfer, 1895). These effects are due in reality to *extract of the posterior lobe* or *pars nervosa* (Howell, 1898). The rise in blood pressure is due to arteriospasm of all the vessels except the renal arteries, which, after a brief period of constriction, dilate. This dilatation of the renal vessels, together with the specific stimulation of the renal epithelium, gives rise to diuresis. The active principle of posterior-lobe extracts, or so-called *infundibulin,* also stimulates contraction of the smooth muscle of the uterus, bladder, intestine and dilator of the pupil, and tends to cause glycosuria, thus resembling closely in its effects the action of epinephrin, though the effects are not identical. Extracts of the pars nervosa exert a galactogogue effect. The normal cerebrospinal fluid probably contains infundibulin, since injection (after slight concentration) produces physiological reactions similar to those following injections of infundibulin itself (Cushing and Goetsch).

The active principle of the posterior lobe is not destroyed by boiling. It is dialyzable through parchment paper; it is not injured by digestion with gastric juice or trypsin; it cannot be a protein and differs from epinephrin; it contains no iodin.

Repeated injections of posterior-lobe extract may be followed by emaciation, due to accelerated metabolism. The aorta undergoes atheromatous change and histological alterations are produced in other ductless glands.

Injections of *extracts of the anterior lobe* (free from pars intermedia) produce no recognizable effects.

We are remarkably ignorant regarding the internal secretion of the anterior lobe. It probably has to do with (1) the growth of bone and (2) the stimulation of the endocrine functions of the gonads that are concerned in the development of the secondary sex characters (*q. v.*).

The *feeding* of extracts of the hypophysis have led, in the main, to negative results, even in young animals.

*Transplantations of the hypophysis* certainly do not survive and remain active unless hypophyseal insufficiency be present, and, even then, survival is doubtful.

*Complete removal* or *destruction of the hypophysis* (Paulesco; Cushing and his associates) is uniformly fatal, being followed in a few days by tremor, fibrillary twitching, arching of the back, slowing of the pulse and respiration, hypothermia, apathy, coma and death—the so-called **cachexia hypophysopriva acuta.** *Partial hypophysectomy* in animals is followed by adiposity, increased carbohydrate tolerance, hypothermia, nutritional changes in the skin and its appendages, sexual inactivity or hypoplasia, retardation of body growth, mental dullness, transient polyuria and histological changes in other ductless glands (Cushing and his associates; Aschner and Biedl).

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## 3. States Due to Over-function of the Hypophysis

*Hyperhypophysism; Hyperpituitarism; Acromegaly; Gigantism*

### (*a*) *Conception of Acromegaly*

Acromegaly is a disease that develops slowly, usually at the end of adolescence. It is due to a hyperfunction of the glandular anterior lobe of the hypophysis cerebri. It causes (1) an increase in the size of the acra (nose, lips, tongue, mandible, hands, feet), (2) hyperplastic changes in the osseous system, (3) certain cerebral and genital symptoms, and (4) certain changes in the other glands of internal secretion (thyroid, genital glands), with corresponding symptoms referable to the autonomic nervous system.

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### (*b*) *Symptoms of Acromegaly*

**Onset.**—The *onset* of the disease may occur in one of two ways. The patient or his friends notice either (1) an enlargement of the hands, feet and face, and a need of larger gloves, hats or shoes than formerly, or (2) certain symptoms like headache, sleepiness, apathy, epileptiform convulsions that bring the person to the physician and lead the latter to suspect the existence of some intracranial lesion. Certain genital disturbances are usually met with at onset also—in *females*, amenorrhea or other menstrual irregularities, in *males* diminished libido and potentia. Such cerebral and genital symptoms may gradually increase over a period of years before skeletal changes are noticed. When the disease is fully developed the bony changes are very marked and the cerebral and genital symptoms are more pronounced.

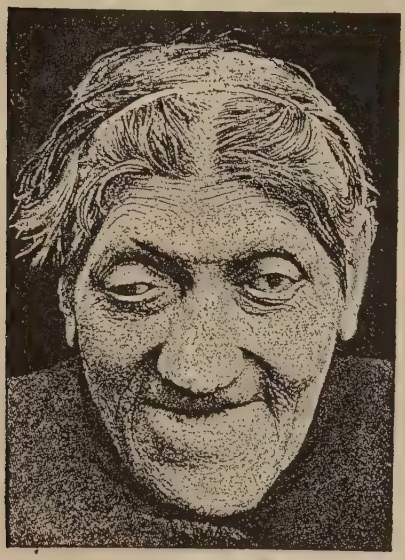

Fig. 660.—Acromegaly. (After P. Marie, "Travaux Scientifiques," published by Masson et Cie, Paris.)

**Changes in the Skeleton and its Coverings.**—These consist chiefly of hypertrophic changes of a peculiar kind in the bones; they lead to characteristic appearances, so characteristic that when one has once seen a typical case of acromegaly, the condition will scarcely be overlooked subsequently.

In the head, the *facial skull* is involved more than the cranial skull, with the resulting ugly distortion known as the acromegalic face (Fig. 660). The *face* is on the whole oval, or hexagonal, and markedly elongated; it is widened somewhat in the transverse direction, all the bones becoming more prominent. The *forehead* looks relatively narrow above the projecting eyebrows and the enlarged orbits. The bones, cartilages and soft parts of the *nose* are enlarged; the nose is often greatly thickened and is usually enlarged in all dimensions. The distance between the *malar bones* is markedly increased and these bones form striking prominences in the acromegalic face. The *eyes* lie deep in the orbits as a rule, though there may sometimes be a protrusion of the eyeballs. The projecting *chin* is characteristic, the bone being thickened and turned upward, as the French say, *en galoche*. The whole face is of the type of the classical profile of the *nut-cracker face* of Punch (Léri). The margin of the *upper lip* is thickened and turned upward. The *teeth* in the lower jaw are shoved

forward in front of those in the upper jaw. The teeth do not change in size, but the spaces between them become widened ("hag teeth"), owing to the enlargement of the jaw, an important and often early sign. Between the malar bones and the chin there are hollows in the cheeks.

The *ears* are enlarged. The *skin,* though thickened, dry and sallow, looks loose and wrinkled; all the natural wrinkles are exaggerated. The *hair, beard* and *eyebrows* are usually heavy and coarse.

The enlargement of the *tongue* may make speech and mastication difficult. The *larynx* becomes enlarged and the voice lower pitched and hoarse. Women, when affected, owing to the marked wrinkling of the skin and low-pitched voice, come to take on a masculine appearance.

The so-called *spadelike hands* are very characteristic. They are broad and thick rather than elongated; the soft parts are greatly enlarged and the folds and sulci are markedly exaggerated ("stuffed" or "pudgy" looking hands). The *fingers* do not taper toward the tips, but are as thick distalward as proximalward, quadrangular at the tips—the so-called sausage-fingers. The size of rings and thimbles has progressively to be increased. The *nails* are short and broad; the lunulae at the bases of the nails are often absent; there is sometimes longitudinal grooving. Deviations from these typical spade hands are sometimes met with, though the common form is that described. The wrists, forearms and arms show relatively little change.

Fig. 661.—Acromegaly. Note the Hexagonal Skull, the Growth of Hair Low in the Middle of the Forehead, the Exaggeration of the Wrinkles, the Spadelike Hands and the Large Feet. (Med. Service, J. H. H.)

In the lower extremities the *feet* undergo modifications similar to those described for the hands, while the legs and thighs are relatively little altered.

In the thorax, the *clavicles* become enlarged and there is usually an outspoken *kyphosis* of the lower cervical and upper thoracic spine. There may be some lumbar lordosis or a variable grade of scoliosis. The *neck* looks short and thick, as though sunken between the shoulders. The *thorax* is thick through from behind forward, but narrowed from side to side. The *ribs* and *sternum* also show hypertrophic changes. Thoracic respiration is inter-

fered with. The *abdomen* projects and the *hips* are broad. The *external genitalia* are usually increased in size in both sexes.

**The Cerebral Symptoms.**—The *headaches* may be very frequent and very severe. They are most often occipital, but they may be frontal, bitemporal or diffuse.

The *mental symptoms* may be pronounced. There is dullness, apathy and general slowing of the mental functions. The patients talk very little, and the speech is heavy and slow; they usually grow sad and irritable. Outspoken psychoses, with melancholic or persecutory ideas, may develop.

In the cases with *epileptiform convulsions,* the attacks may be those of *grand mal* or of *petit mal.* Rolleston reports the death of an acromegalic during an epileptiform attack, and a similar exitus has been described by other authors.

If a *bitemporal hemi-anopsia* exist, it is most helpful in diagnosis, since it points to a lesion of the middle part of the optic chiasm, a lesion most often due to hypophyseal tumor. *Optic atrophy* and *choked disk,* when diffuse, are due to the general *increase of intracranial pressure.* Careful studies of the *visual fields* by the perimeter are important for diagnosis in the early stages of the disease.

**The Genital Symptoms.**—In men, the *external genitalia,* with the exception of the scrotum and testes, are often hypertrophied, but there is *diminution of libido and potentia.* In women, *amenorrhea* is often an early symptom, and it is usually persistent. The *external genitalia* are hypertrophied, but the *uterus* is small and the *breasts* flabby and pendulous.

**Other Symptoms of Acromegaly.**—In the *respiratory system,* emphysema and chronic bronchitis are not uncommon. In the *cardio-vascular apparatus,* the heart is often found hypertrophied, apparently as part of a general splanchnomegaly. Examinations of the *urine* have shown the frequency of glycosuria (30-50 per cent of the cases), which may or may not be accompanied by other signs of diabetes mellitus (polydipsia, polyphagia, etc.). A number of acromegalics have died in diabetic coma (Hinsdale). Albuminuria is rare. There appears to be a retention of phosphates and of lime salts (Edsall and Miller), possibly associated with the overgrowth of bone.

In an acromegalic, in Janeway's clinic, Hamman has recently demonstrated a blood-sugar curve after the ingestion of 100 g. glucose that differs from the curve in a normal person by its greater height and longer duration.

As Cushing has emphasized, a primary hyperpituitarism with acromegaly or gigantism may be followed later on by a *terminal hypopituitarism,* the change appearing to depend upon a cystic retrogression of the primary glandular hyperplasia.

Examinations of the *blood* often reveal a mononucleosis and an eosinophilia.

**The Other Glands of Internal Secretion in Acromegaly.**—The *thyroid* usually shows certain abnormalities (struma, atrophy). The *thymus* may be enlarged and a complicating status lymphaticus has been observed. In the diabetic cases the functions of the internal secretion of the *pancreas* are probably involved.

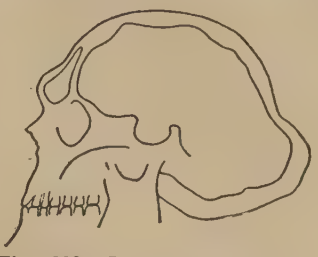

Fig. 662.—Diagram of a Röntgenogram of the Skull in Acromegaly. Note the Enlargement of the Sella Turcica; the Irregularity in the Thickness of the Skull Bones; the Enlargement of the Forehead and Protrusion of the Superciliary Ridge; the Prominence Behind the Lambdoid Suture above the External Occipital Protuberance. (After Béclère in A. Léri, "Handb. d. Neurol.," published by J. Springer, Berlin.)

**Symptoms in Acromegaly Referable to the Autonomic Nervous System.**—The *tonus* in both the sympathetic and the craniosacral autonomic systems may be altered, either in the direction of increase or of decrease. It seems probable that the internal secretion of the hypophysis has a direct effect upon the vegetative nervous system (see above under physiology), but doubtless some of the symptoms in the domain of the vegetative nervous system in acromegaly are due to the secondary disturbances of other endocrine glands, especially the thyroid.

**X-rays of the Sella Turcica in Acromegaly.**—The sella turcica is usually enlarged. Sometimes, the partition between the sella and the sphenoidal cavity is broken through. In other cases, the clinoid processes are destroyed. Now and then an acromegalic yields a normal röntgenogram of the sella. For a further description, see below under Diagnosis.

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### (*c*) *Special Clinical Forms of Acromegaly*

Léri, reviewing the bibliography, distinguishes several special forms: (1) a painful form; (2) an amyotrophic form; (3) a form associated with gigantism; (4) a form associated with obesity; (5) a form associated with trophedema or with myxedema; and (6) a form accompanied by severe nervous or mental symptoms.

**The painful form of acromegaly.**—In this form, pains dominate the clinical picture. All acromegalics have headache, but at least half of them suffer from other pains in the trunk or limbs. Two sub-types are recognized, (a) the *rheumatic painful type,* involving the joints, and (b) the *neuralgic* or *hyperalgic type,* involving the nerve trunks (*acromegalic pseudo-tabes*).

**The Amyotrophic Form of Acromegaly (Duchesnau).**—In this form, an extensive *amyotrophia* occurs in all four extremities, without DeR, and with no change, or only slight diminution, in the reflexes.

**Acromegaly with Gigantism.**—Most acromegalics are taller than normal. Nearly half of all giants become acromegalic. It is probable that *gigantism* is due to hyperpituitarism in childhood; that *acromegaly without gigantism* is due to hyperpituitarism after youth; and that *acromegaly with gigantism* is due to a hyperpituitarism beginning in childhood and continuing into adult life. Thus a giant may become an acromegalic, but an acromegalic of small stature can never be changed into a giant.

**Acromegaly with Obesity.**—Here, the obesity is probably the result of a terminal hypopituitarism, superimposed upon a preceding hyperfunction of the gland.

**Acromegaly with Chronic Trophedema or with True Myxedema.**—In this form, we see a combination of the symptoms of acromegaly with those of *trophedème,* or with those of *myxedema.*

**Acromegaly with Outspoken Nervous or Mental Disease.**—In this form, the acromegaly is accompanied by profound *nervous* symptoms (epilepsy, brain tumor), or severe mental symptoms (mania, melancholia, delusions, etc.).

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### (d) *The Course of the Disease*

Acromegaly is a slow but a progressive process, beginning usually in the early twenties. Those affected may live from ten to thirty years. In very severe cases, death may occur in three or four years; in the more benign cases, a patient may live fifty years after the onset. Even centenarian acromegalics have been recorded. Toward the end, a progressive *cachexia* develops; the patients lose weight and grow ever weaker. Death may occur in an epileptiform attack, in diabetic coma, from cardiac failure, or from some complication, especially pulmonary tuberculosis.

### (e) *Etiology and Pathogenesis of Acromegaly*

Though the disease is undoubtedly due to a disturbance of the function of the hypophysis cerebri, the causes of the *hypophyseal disease* are not fully known.

*Women* are affected more often than men. The disease begins between youth and middle life (20th to 40th year); rarely, the disease may set in earlier, or very late in life. It seems to run in *families*, though since the disease begins in youth and, once developed, almost invariably causes sterility, acromegalics have but few descendants. The occurrence of gigantism in families in which acromegaly exists has often been noted.

An analysis of the previous history of acromegalics reveals the frequency of *disturbances of metabolism* (gout, diabetes), of certain *infections* (polyarthritis, typhoid, scarlet fever, etc.), and of certain *intoxications* (potatorium, lead poisoning).

Post mortem studies have revealed hypophyseal lesions almost constantly in the form of a *tumor*. This was formerly believed to be sarcoma, but more recent studies indicate that the neoplasm is nearly always an *epithelioma*. The cells formerly taken to be the round cells of sarcoma have been found to be deformed epithelial cells of the hypophysis. The epithelium has its origin in the glandular

cells of the anterior lobe. The *flat celled epithelial tumors* of the hypophysis do not cause acromegaly. It has been asserted that acromegalic phenomena are, however, *not always due to tumor*, but may be associated with (1) *cysts*, (2) *hemorrhages*, (3) *cirrhotic processes*, etc., but, in such cases, there is sometimes a neoplasm in an *accessory hypophysis* (in the pharyngeal wall or in the sphenoidal bone); or the case may have been one of *syringomyelia* with cheiromegaly, of so-called *pseudo-acromegaly*, or of *mere gigantism*. Cantani has collected 30 cases in which there was neither tumor nor histological change in the hypophysis.

Some changes are always present in *other glands of internal secretion* (thyroid adrenals).

The *splanchnomegaly* involves the heart, the liver, the spleen, the pancreas and the kidneys, but the brain does not become enlarged and the genital organs atrophy. The ossification of the spinal meninges, sometimes found, may be the cause of the neuralgic pains in the "painful type" of acromegaly.

Marie's theory that acromegaly is a *systemic dystrophy of hypophyseal origin* is the view generally adopted. There is much to be said in favor of a hypothesis, according to which, at the beginning of the disease, we have to deal with a *hyperfunction* of the hypophysis, and, later on, a *hypofunction* appears as a result of the degenerative and destructive character of the later lesions (Tamburini; Béclère). Recently, writers have rallied to the support of Roussy's doctrine, according to which the disease is due, neither to an increase nor to a diminution of the secretion, but to a perversion thereof—a *dyspituitarism* or a *dyshypophysism*.

Whether the abnormal secretion causes acromegalic changes by acting directly upon the bony and cartilaginous tissues, or indirectly through their trophic centers in the nervous system, is not known. The amenorrhea and other genital disturbances, and the glycosuria of acromegalics, are probably due to excess of the secretion of the posterior lobe. The experiments of Goetsch, Cushing and Jacobson upon the relations of the functions of the posterior lobe to carbohydrate tolerance are very convincing. The obesity sometimes met with in acromegaly, especially in its later stages, appears to be due to hypohypophysismus, and especially to secretory insufficiency of the posterior lobe.

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### (f) *The Diagnosis of Acromegaly*

The outspoken cases of acromegaly are easily recognizable, but the beginning cases are often overlooked. Complaints of *severe headache*, of *neuralgic pains* in the limbs, of *genital disturbances* in the early twenties, should always excite suspicion, particularly in families of *tall* people.

Prominent supra-orbital ridges, thick lips, widened spaces between the incisor teeth, large pawlike hands, should lead one to investigate carefully the hypophyseal functions.

In doubtful cases, *röntgenograms of the skull* should always be made, when one or more of the following important changes may be observed: (1) enlargement of the anteroposterior, or of the vertical, diameter of the sella turcica; (2) enlargement of the frontal sinuses; (3) irregularity in thickness of the calvarium; (4) exaggeration of the external occipital protuberance.

This so-called *radiographic formula* is at present the most certain proof of the existence of acromegaly (Léri).

### (*g*) *Differential Diagnosis of Acromegaly*

Acromegaly affects both the head and the extremities, and may be confused (1) with diseases that affect all these, (2) with others that affect the head alone, and (3) with still others that affect the extremities only.

#### i. From other Diseases that Modify the Form of the Head as well as of the Extremities

We must differentiate acromegaly: 1. From *myxedema* (soft parts infiltrated, arrest of development of bones; often dwarfism, absence of enlargement of the bones, full-moon face).

2. From *Paget's disease* (cranial skull rather than facial bones affected; bitemporal diameter of skull broadened rather than bimalar diameter; face triangular, with base above, rather than hexagonal; enlargement of shafts of bones rather than of acra; characteristic cotton-batting appearance in x-ray pictures; calcification of arteries; advanced life).

3. From *rickets* (enlargement of skull due to projecting frontal and parietal bones; late closure of fontanelles; small senile face; shortening and curving of long bones of extremities; enlargement of distal extremities of long bones; absence of changes in acra; rickety rosary; frequent dwarfism; disease of childhood).

#### ii. From other Diseases Affecting the Head but not the Extremities

Of these diseases we must differentiate acromegaly: 1. From *oxycephaly* or so-called *tower skull* (head lengthened in vertical direction, but flattened dorsally; no contraction of visual fields; beginning in childhood; characteristic radiographic formula).

2. From *leontiasis ossea* (complete integrity of soft parts; nose sunken between hypertrophic bony masses, giving the appearance of a lion's face; hypertrophic changes in bones of face and skull occur rapidly; disease of youth; tongue not enlarged).

#### iii. From Diseases Resembling Acromegaly, but Affecting as a Rule the Extremities Only

Of these diseases, we must differentiate acromegaly: 1. From the *hypertrophic pulmonary osteoarthropathy* of P. Marie (bones of hands enlarged, especially

at tips of fingers, with incurved nails, but soft parts not hypertrophied; enlargement of wrist-joint; similar changes in the toes and ankles; dorsolumbar rather than cervicodorsal kyphosis; margin of upper jaw hypertrophied but mandible unaffected; absence of genital and cerebral symptoms; association with intrathoracic diseases.

2. From *syringomyelic cheiromegaly* (characteristic objective sensory symptoms; trophic and vasomotor changes; absence of alterations in the skull).

Wherever possible the diagnosis of the size and exact position of the tumor of the hypophysis should be made, inasmuch as this may decide whether or not the treatment shall consist of an attempt at hypophysectomy either by the intracranial or extracranial route, or must be limited to radiotherapy, opotherapy, or symptomatic treatment.

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## 4. States Due to Under-function of the Hypophysis

*(Cachexia hypophysopriva, Hypo-hypophysismus, Hypopituitarism, Hypophyseal Dystrophia adiposogenitalis)*

The phenomena of *cachexia hypophysopriva* have been referred to in the introductory paragraph. We shall deal here especially with the condition first clearly characterized in 1901 by A. Fröhlich, and since known in the literature as **typus Fröhlich** (quickly developing obesity; infantilism of the genitals; myxedemalike changes in the skin), now usually described as *hypophyseal dystrophia adiposogenitalis.*

### (*a*) *Conception of Dystrophia adiposogenitalis of Hypophyseal Origin*

This is a well-characterized clinical syndrome, not infrequently met with in human beings, and corresponding to the *typus Fröhlich* men-

tioned above. It is due, as a rule, to a tumor or other disease of the hypophysis, resulting in a decrease of the functional activity of that gland, especially in its posterior lobe. The disease has been produced experimentally by partial extirpation of the hypophysis in young animals (Cushing, Aschner).

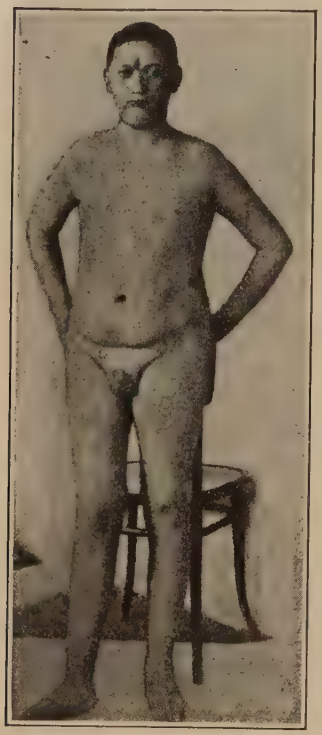

Fig. 663.—Von Fröhlich's Case of Hypophyseal Obesity after Operation. (After A. Biedl, "Innere Sekretion," published by Urban & Schwarzenberg, Berlin.)

### (*b*) *Symptoms of Dystrophia adiposogenitalis*

When the syndrome is due to tumor of the hypophysis the following phenomena are usually met with:

I. Symptoms directly due to the brain tumor:
   (a) *General symptoms* due to increased intracranial pressure (headache, mental disturbances, vomiting, etc.).
   (b) *Neighborhood symptoms* due to local pressure (optic atrophy, bitemporal hemi-anopsia, contractions of visual fields, changes in sella turcica, lesions in body of sphenoid bone.

II. Symptoms due to loss of function of the hypophysis (obesity, falling out of hair, faulty skeletal development, polyuria, trophic changes in the skin, etc.).

#### i. Symptoms Directly Due to the Brain Tumor

**General Symptoms Due to Increased Intracranial Pressure.**—*Headache* is often a prominent symptom, occurring in at least one-third of the cases. It varies in intensity and in localization, but is often bitemporal or frontal, sometimes diffuse. *Vomiting* and *dizziness* are not uncommon, and may accompany the headache. *Mental symptoms* of variable character occur. The patients impress one as being below par mentally. There may be outspoken signs of mental disturbances (excitement, depression, psychoneurotic phenomena, or even hallucinations). As a rule, however, the patients are remarkably quiet and resigned, bear pain well, and coöperate easily with the physician (von Frankl-Hochwart). A tendency to *narcolepsy* has been observed in several cases. *Epileptiform attacks* may

be due either to the general increase in pressure, or they may be neighborhood symptoms. In the latter case, especially if the gyrus hippocampi be irritated, *hallucinations of taste and smell* may characterize the aura at the beginning of an attack.

**Neighborhood Symptoms Due to Local Pressure.**—These are referable partly to the cerebrum, partly to the base of the skull and the nasopharynx.

Among the cerebral nerves that may be injured are (1) the *N. opticus*, (2) the *eye muscle nerves* (III, IV, VI), more rarely (3) the *Nn. olfactorii*, (4) the *N. trigeminus* and (5) the *N. facialis*.

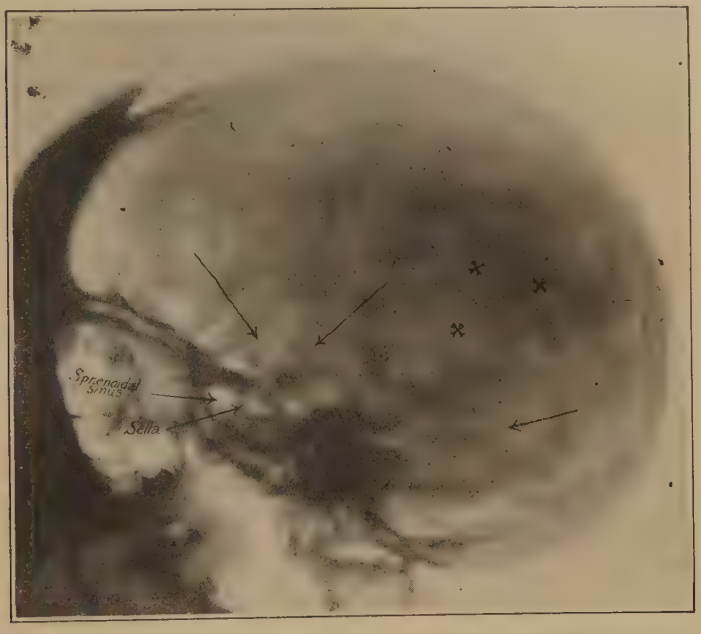


Fig. 664.—Teratoma of the Hypophysis cerebri. Note also the Dilated Lateral Sinus, and the Open Sutures. The +'s Mark Internal Hydrocephalus. (X-ray Dept., J. H. H.)

The commonest and most serious neighborhood symptoms are the *visual disturbances*, depending upon *optic nerve lesions*, especially lesions of the chiasm. The visual disturbance is usually bilateral. *Primary optic atrophy* is present in over half the cases; this is associated with *choked disk* in about one-third of the cases. *Bitemporal hemi-anopsia* is common, homonomous hemi-anopsia rare.

The injury to the eye-muscle nerves may be evident as *diplopia*. The N. oculomotorius is much more often affected than the N. abducens. *Nystagmus* is not uncommon.

Disturbances of smell, taste and sensation on the face are rare, and facial palsy is uncommon.

Of the symptoms referable to other portions of the *base of the brain* may be mentioned: (1) *spastic paralysis* with positive Babinski, due to involvement (often bilateral) of the cerebral peduncles; (2) *polyuria;* and (3) disturbances of temperature regulation (*hyper-* or *hypothermia*), the latter symptoms being referable perhaps to injury to the tuber cinereum or adjacent parts.

Of the signs referable to *changes at the base of the skull and in the nasopharynx* may be mentioned:

1. *Alterations in the x-ray picture of the sella turcica* due to the hypophyseal tumor. When the tumor is *intrasellar* in origin there is even enlargement of the sella, its floor becomes deeper and thinner and seems to be nearer the floor of the middle fossa of the skull. The back of the saddle is thinned, reclined and lengthened. There is an acute-angled projection at the point where the contour of the sellar fossa goes over into the planum sphenoidale. The anterior clinoid process may look normal

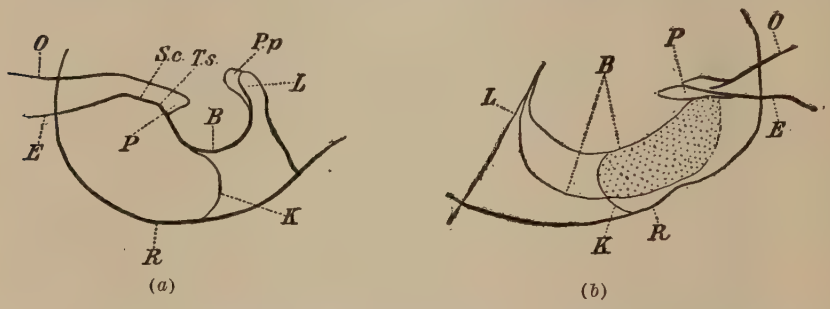


Fig. 665.—(*a*) Shows the Outline of a Röntgenogram of a Normal Sella Turcica. (*b*) Shows a Large Tumor of the Hypophysis, Accompanied by a Dystrophia adiposogenitalis, and Causing Flattening of the Sella Turcica. The Floor of the Sella (B) Presents a Double Contour, Indicating an Asymmetrical Pressure of the Tumor Against the Base of the Skull. B = Floor of Sella; E = Planum sphenoidale; K = Sphenoidal Sinus; L = Pommel; O = Roof of Orbit; P = Processus clinoideus anterior; Pp = Processus clinoideus posterior; S.c. = Sulcus chiasmatis; T.s. = Tuberculum sellae. (After A. Schüller, "Handb. d. Neurol.," published by J. Springer, Berlin.)

or it may be very "plump"; sometimes it is pressed upward and hollowed out on its lower surface. In tumors of *extrasellar* origin there is a flat, bowl-like expansion of the sella, with thinning and shortening of the back of the saddle, sharpening, or shortening, of the anterior clinoid process, and erosion of the tuberculum sellae so that the floor of the sella, though looking thin, does not seem to be much nearer the floor of the middle fossa of the skull, and it forms an oblique angle at its junction with the planum sphenoidale. If the tumor be very *large* it may cause such widespread destruction of the body of the sphenoid bone that one can no longer decide whether it has been intrasellar or extrasellar in the beginning (Erdheim, Schüller).

Owing to the increased intracranial pressure the impressiones digitatae

of the skull may be deepened and the general wall of the skull thinned. Occasionally, calcified or ossified nodules in the tumor itself are visible in the x-ray plate.

2. *Nasopharyngeal symptoms* may include (a) epistaxis, (b) rhinorrhea nasalis, (c) suppurative sphenoidal sinusitis with polyp formation, (d) extension of tumor into nasopharynx, recognizable by inspection and palpation.

### ii. Symptoms Due to Lessened Internal Secretion of the Hypophysis

(*Hypopituitarism*)

**Obesity.**—Accumulations of fat may be enormous, the *body weight* in adults reaching 200 or 300 pounds. The fat is most abundant as a rule on the abdomen and thighs, but may be generally distributed. As a rule the fat is not tender.

**Changes in the Hair.**—When the disease occurs in the young, the hairs of the axilla (*hirci*) and those of the mons veneris (*crines pubis*) are scanty or absent. In males, the hairs of the *beard* may also be scanty and the distribution of the hairs of the body may resemble that met with in the female (*typus femininus*). In the female, on the contrary, the distribution of hair may approach the masculine type.

These peculiarities of the secondary sexual character go along with a hypoplastic or infantile state of the *genitalia* in cases in which the disease sets in before puberty. If the disease appear after puberty, the secondary sex features may undergo retrogressive changes (falling out of eyebrows, hirci and crines pubis).

**Faulty Skeletal Development.**—In some cases of early hypopituitarism, *dwarfism* is met with (Aschner), due to faulty function of the anterior lobe.

If the disease develop before puberty, the *skeleton* in males assumes the feminine type (broad pelvis, genu valgum, sometimes with coxa vara and pes valgus).

The extremities are often gracile, the fingers tapering.

**Polydipsia and Polyuria (Diabetes insipidus).**—This is present in many of the cases (see Part XIII). On the other hand, glycosuria is very rare, the patients often exhibiting a very high grade of carbohydrate tolerance (Cushing).

**Trophic Changes in the Skin.**—The skin is pale, usually thin, soft and smooth. Sometimes it is wrinkled. In a few cases it may resemble that in myxedema or in scleroderma.

**Symptoms Referable to Other Endocrine Glands.**—Tachycardia, asthenia, arterial hypotension, abnormal pigmentations, and myxedema, when present in association with dystrophia adiposogenitalis, are probably

due not directly to the hypopituitarism but indirectly to disturbances of the other endocrine glands (thyroid, chromaffin system).

The evidence at present favors the view that the growth disturbances, the genital infantilism and the temperature anomalies are related to loss of function of the *anterior lobe*, and that the obesity, increased carbohydrate tolerance, the polyuria and the arterial hypotension depend upon loss of function of the *posterior lobe* and the *pars intermedia*.

### (c) *Diagnosis of Dystrophia adiposogenitalis*

In *typical cases* with (1) trophic disturbances (obesity and genital atrophy, (2) visual disturbances (bitemporal hemi-anopsia), and (3) excavation of the sella turcica in the x-ray picture, the diagnosis is easy.

In atypical cases (*formes frustes*), and at the beginning of the disease, great difficulty may be experienced. Any one of the following symptoms by itself should excite suspicion: (1) limitation of the visual fields on the temporal side, (2) menstrual disturbances, (3) rapidly appearing obesity, (4) signs of increased intracranial pressure, (5) diabetes insipidus. In such cases an x-ray examination of the sella turcica should not be omitted. Excavation of the sella, when demonstrable, is most often due to hypophyseal tumor, but may be caused by aneurism, or by tumors of the adjacent dura or brain.

Though bitemporal hemi-anopsia is most often due to hypophyseal tumor, it occurs sometimes in tabes and in lues cerebri.

It must not be forgotten that tumor of the hypophysis, though usually associated with obesity and genital atrophy, sometimes occurs without these symptoms.

Sudden remissions of the symptoms suggest a cystic lesion or a luetic lesion of the hypophysis.

In **differential diagnosis,** brain tumors other than those originating in the hypophysis, hydrocephalus internus, epilepsy, and diseases of the base of the skull should be considered. Among the endocrinopathies that sometimes resemble dystrophia adiposogenitalis, one should keep in mind Dercum's disease, chlorosis, myxedema, cretinism, status thymicolymphaticus, the various forms of dwarfism, and the so-called polyglandular syndromes.

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## E. Diseases of the Corpus pineale, or Epiphysis cerebri, and Its Neighborhood

*(The Epiphyseopathies)*

### 1. Anatomical and Physiological Notes

The *epiphysis cerebri,* or *corpus pineale,* if evidence recently brought is to be believed, manufactures an internal secretion that is related to the maturation of the body, influencing apparently the whole bodily and mental development. Over 60 cases of diseases of this structure have been published. In many instances it is possible to make the diagnosis of disease of the pineal body *intra vitam.*

The histological structure of the organ is well described in Marburg's paper (1913). Physiologists, despite numerous experiments, seem to have been unable to throw light upon the functions of the epiphysis. Our knowledge of its importance has been derived from the studies of clinicians and pathologists.

The corpus pineale is often the site of cyst formation and of tumor

formation. In the latter instance, teratoma is most common, though glioma is not infrequent. Cysts and tumors of the epiphysis lead to compression of the vena magna Galeni and of the aqueduct of Sylvius, frequently giving rise to a high grade of hydrocephalus internus of the third ventricle and of the lateral ventricles.

My own opinion is that the pineal body need not produce an internal secretion, but that tumors of this structure may exert neighborhood influences that lead to abnormal functioning of distant endocrine glands, especially of the gonads.

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## 2. Clinical Studies of Disease of the Pineal Body

### (*a*) *Symptoms of Cysts and Tumors of the Pineal Body and Its Neighborhood*

These include (1) symptoms of increased intracranial pressure, (2) certain focal symptoms, and (3) certain signs of disturbed internal secretion of the epiphysis.

The signs of *increased intracranial pressure* depend upon the internal

hydrocephalus that develops, rather than directly upon the tumor. They include headache, vertigo, vomiting, choked disk, drowsiness and certain mental changes. It is unusual to have bradycardia.

The *focal symptoms* usually refer to the region of the midbrain. They include paralyses of the N. oculomotorius, the N. trochlearis and the N. abducens; these are usually accompanied by diplopia. Nystagmus and exophthalmos are occasionally observable. Optic atrophy is not uncommon, due to compression of the optic chiasm from dilatation of the third ventricle. Other cerebral nerves, including the N. facialis, the N. acusticus, and the N. glossopharyngeus, may be involved.

When polyuria and polydipsia are present they are probably due to pressure upon the hypophyseal region. Polyphagia may be a marked symptom.

The symptoms depending upon *disturbance of the internal secretion* of the epiphysis include (1) premature puberty (*pubertas precox*), and (2) changes in the carbohydrate tolerance.

A child of four or of six years of age may exhibit fully developed genitals with pubic and axillary hair like those of an adult, and with emotional and intellectual states corresponding. In boys, the penis may reach an unusual size, especially in teratoma cases.

Marburg is of the opinion that the function of the internal secretion of the pineal body is to inhibit the ripening of the organism, and that in glandular insufficiency this inhibition is taken off and premature puberty results. Munzer suggests that the epiphysis inhibits the hypophysis, and that, normally, an epiphyseal insufficiency develops at puberty, leaving the hypophysis free to bring about the maturation of the organism. The close relations of the hypophysis, the epiphysis and the gonads is certain, but requires further study.

To me it is conceivable that lesions of the epiphysis may act upon distant endocrin glands through the excitation of nerve paths near it. Such a view need not postulate the existence of an internal secretion formed by the epiphysis itself.

The *carbohydrate tolerance* and the *body weight* may be markedly affected. In some of the cases there has been extreme obesity; in others, marked general cachexia with emaciation. Some have thought that the obesity is due to a *hyperpinealism* and that the cachexia with emaciation depends upon *apinealism*. It would seem to be possible that, in both instances, we may be dealing, not with a primary epiphyseal defect, but rather with a secondary hypophyseal influence.

A majority of the cases of disease of the pineal body have occurred in early life (before 30) and have run an unfavorable course, death usually occurring within a few months or years after the appearance of symptoms.

### (*b*) *Diagnosis of Involvement of the Pineal Body in Disease*

If a young person present (1) signs of increased intracranial pressure, (2) focal symptoms pointing to the midbrain region, and (3) abnormal

height, unusual growth of hair, obesity, drowsiness, and premature sexual development (bodily and psychic), a tumor of the pineal gland is probably the cause of it (von Frankl-Hochwart).

In *differential diagnosis* we must distinguish disease of the pineal body (1) from *hypophyseal tumors* (bitemporal hemi-anopsia, röntgenogram of sella turcica), and (2) from *other causes of precocious puberty* (neoplasms of the genital glands and of the interrenals).

Symptoms not unlike those due to pineal body tumor may be due to tumors in the neighborhood (midbrain, cerebellum), or to chronic internal hydrocephalus.

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# F. Diseases of the Chromaffin System and of the Interrenal System

*(The Chromaffinopathies and the Interrenopathies)*

## 1. Anatomical-Physiological Introduction

The *chromaffin system* includes the medulla of the suprarenal glands, the paraganglia, and certain microscopic accumulations of similar tissue in the sympathetic ganglia. The chromaffin system includes also the carotid gland, the large chromaffin body of the plexus ganglia, and the so-called accessory body

(*Nebenkörper* of Zuckerkand). All this tissue is derived originally from sympathetic nerve cells. The tissue is called *chromaffin* on account of its affinity for the chrome salts of fixing fluids. Physiologically, the chromaffin tissue produces epinephrin or adrenalin and gives it to the blood.

The cortex of the suprarenal glands and certain similar tissues elsewhere do not belong to the chromaffin system, but to the so-called *interrenal system* (See below). In lower animals, the interrenal organs remain permanently separated from the suprarenal organs, or chromaffin system, but in higher vertebrates and in man a group of the suprarenal and interrenal bodies unite to form the *suprarenal gland,* though certain isolated interrenals and certain isolated chromaffin masses also persist, these being more abundant before puberty than afterward. In human beings, the interrenal system largely disappears, except for the cortex of the suprarenal glands. Minute masses, however, the size of a pin's head, may be found in the sympathetic ganglia in the hilus of the kidney, in the prostate, in the broad ligament, in the inguinal canal, in the epididymis, and along the spermatic veins.

The chief *function of the chromaffin system* appears to be the production of epinephrin and the continuous supply of this substance to the blood, through which it acts upon the sympathetic nervous system, helping to maintain blood-

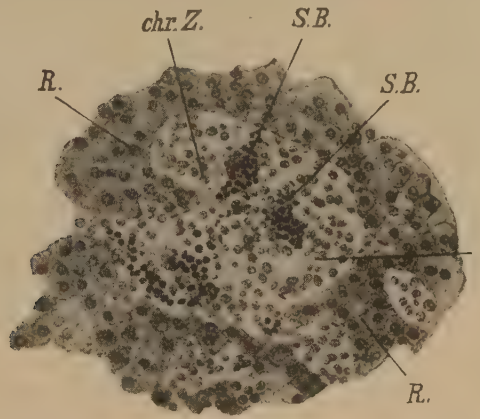


Fig. 666.—Anlage of Adrenal in Human Embryo 95 mm. Long. 150 ×. R. = Cortical Cells. S.B. = Cells from Sympathetic Nervous System. chr.Z. = Chromaffin Cells. (After Wiesl in A. Biedl's "Innere Sekretion," published by Urban & Schwarzenberg, Berlin.)

pressure and sympathicotonus in general (Elliot). The epinephrin seems to act upon a structure intermediate between the nerve ending and the smooth muscle; it is often described as a "sympathetic hormone."

The epinephrin-production of Zuckerkandl's accessory body, and in the dog of the large abdominal paraganglion, seems to be precisely similar to that of the medulla of the suprarenal gland itself.

On account of the pigmentation, the digestive disturbances and the asthenia that occur in Addison's disease, the best-known malady involving the suprarenal gland, it is assumed that, in some way or another, this chromaffin system controls the distribution of pigment in the skin, the feelings of muscular weakness, etc.

The cortex of the suprarenal glands is of epithelial origin and belongs to the interrenal system. This interrenal system is necessary to life, though its functions are as yet but poorly understood. The tissue is known to produce *cholin,* a sub-

stance that lowers blood pressure, but cholin is also produced by the thymus gland. Over-activity of the interrenals seems to be the cause of the *remarkable*

Fig. 667.—Adrenal of a Dog Transplanted 78 Days in the Parenchyma of the Kidney. 8 x. The Chief Mass is Regenerative Hypertrophy of the Cortex; in the Center is the Medulla Stained Brown with Chromic Acid. Below, at the Left, is the Glandular Structure. (After v. Haberer in A. Biedl's "Innere Sekretion," published by Urban & Schwarzenberg, Berlin.)

*sexual disturbances* (pseudohermaphroditism, premature sexual maturity, virilismus), that occur in connection with hyperplasias and tumors of the cortex of the suprarenal glands.

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## 2. Anomalies of the Chromaffin System and of the Interrenal System

We are beginning clinically to recognize (1) the phenomena of *under-function of the chromaffin system,* associated with hypoepinephrinemia, and (2) the phenomena of *over-function of the chromaffin system,* associated with hyperepinephrinemia.

The states of under-function have, however, been much more carefully studied thus far than the states of over-function. The under-function depends, in some cases, chiefly upon a *congenital inferiority* of the chromaffin system, a fault of the constitution. A very high grade of congenital inferiority is incompatible with life. Less severe grades, however, are compatible with life, but lead to the development of characteristic symptoms (*primary insufficiency* of the chromaffin system), usually associated with status hypoplasticus, or status thymicolymphaticus (*q. v.*). In other instances the congenital inferiority of the chromaffin system, perhaps in-

sufficient to cause marked symptoms in itself, predisposes to the localization of certain diseases in the chromaffin organs, especially tuberculosis (88 per cent of the cases), syphilis, and various acute infections; when these injuries are superimposed upon the congenital inferiority of the system, the symptoms of under-function appear (so-called *secondary insufficiency* of the chromaffin system).

The cases of outspoken congenital inferiority of the chromaffin system will be described under the caption *Status thymicolymphaticus* (see below). The cases of combined congenital inferiority with acquired injuries to the chromaffin system are best described under the caption *Addison's disease.*

### (*a*) *Addison's Disease*

#### i. Historical Note

Addison, in his publication of 1855, gave a masterly description of the disease now known by his name. He described it as an idiopathic anemia related to disease of the suprarenal bodies, characterized by a bronzing of the skin, digestive disturbances, and nervous disturbances, leading to chronic cachexia, and ending fatally.

#### ii. Etiology of Addison's Disease

The disease is rare. *Men* are more often affected than women. As to *age,* it occurs most often between 20 and 40, being rare before 15 and after 60. Among *predisposing factors* may be mentioned: depressing conditions of life, alcoholism, infections, intoxications, trauma and heredity. In all cases, probably, there is a *congenital anomaly* of the chromaffin system, consisting of an anatomical and functional inferiority of the chromaffin tissues, usually associated with some hypoplasia of other organs (vascular system, genitalia), and with some signs of status thymicolymphaticus (persistent thymus; large tonsils; peculiarities in distribution of the body hair). In most of the cases examined, *tuberculosis* of the suprarenal glands has been found at autopsy. In other cases, *syphilis* or *atrophy* of these glands has been observed; in a few cases, no anatomical lesion of the chromaffin system has been demonstrable, and a pure *functional disturbance* had to be assumed.

#### iii. Symptoms of Addison's Disease

**Onset.**—The *onset* is insidious, beginning with fatigability, muscular weakness (*adynamia, asthenia*), and disinclination for exertion. Sooner or later pigmentation of the skin (*melanoderma*) and of the mucous membranes appears. About the same time *digestive disturbances* may also set in (gastralgias, hyperacidity, nausea, disturbances of appetite and of

bowel movement). Certain *nervous disturbances* may also appear (neuralgic pains, headache, dizziness, fainting spells, insomnia, mental depression or excitation). Outspoken *arterial hypotension* is a common finding. The patients are often dyspneic without apparent cause. Menstrual disturbances occur in women and sometimes impotence in men.

**Course.**—The *course* of the disease is, as a rule, exceedingly chronic, extending over several years, the symptoms being mild at first, with intermissions, but toward the end severe (extreme asthenia, anorexia, uncontrollable vomiting, diarrhea, delirium, coma, death).

**Asthenia.**—The *adynamia* or *asthenia* of the disease is striking. When outspoken, the patients lie almost in a stupor, apparently unable to move, to speak or to eat. It is both a physical and a psychic adynamia. The patients as a rule lack energy and lose interest in everything. The memory is enfeebled. Less often, one sees states of excitation; then the patients may be irritable, egocentric, and quarrelsome. Insomnia is a troublesome symptom, though it may alternate with periods of great drowsiness. The tendency to fainting seems to be a part of the general adynamia.

**Digestive Symptoms.**—The *digestive disturbances* are usually a prominent feature, though in a few cases they have been entirely absent. They include meteorism, abdominal tenderness, abdominal pains (diffuse, epigastric, or perirenal), anorexia, nausea, vomiting, hyperacidity, and constipation or diarrhea. In some cases there is abnormal hunger, at the beginning, often associated with polydipsia and polyuria.

**Pigmentation.**—The *melanoderma* comes on gradually. It may be the first symptom. The skin assumes a dirty yellow tint, later changing to light brown, to deep dark brown, and, finally, to a deep black color. The pigmentation may show a bluish or a greenish tint (Wiesel). The pigmentation may be diffuse, though certain special areas of the skin are darker than others (axillae, nipples, genitals, extensor surfaces of joints, and parts exposed to pressure, like the neck, the waist and the shoulders). Especially important is the pigmentation of the folds of the palms of the hands and of the flexor surfaces of the small joints of the fingers, and the appearance of spots of pigmentation on the mucous membrane of the mouth, lips and palate. In rare cases of Addison's disease, there is no abnormal pigmentation whatever. The conjunctiva and the finger nails are rarely pigmented, and the hair itself does not undergo pigmentary change. Blondes as well as brunettes may suffer from Addison's disease.

**Other Symptoms.**—Among the *other symptoms* of importance may be mentioned: (1) peculiar pains in the lumbar region (perirenal), (2) sometimes stenocardiac attacks (coronary hypoplasia), (3) low blood pressure (hypoepinephrinemia), (4) marked subjective feelings of dyspnea, (5) often eosinophilia, and sometimes lymphocytosis (von Neusser), (6) sometimes the appearance of amino-acids and of an increase of the volatile fatty acids in the urine.

### iv. Diagnosis of Addison's Disease

This is easy when the *typical triad* of symptoms (asthenia, digestive disturbances, melanoderma) is present, but it may be exceedingly difficult in the atypical cases (*formes frustes*).

In doubtful cases, attention to the following points should be helpful:

(1) the presence of constitutional anomalies corresponding to the status thymicolymphaticus, (2) exact studies of the pigmentation of the body, (3) a careful analysis of any digestive disturbances present.

Cases of *Addison's disease without pigmentation* are very apt to be overlooked. On the other hand, there are many diseases that have nothing to do with Addison's disease, but which lead to pigmentation that may be mistaken for that of Addison's disease. Among these, we must differentiate Addison's disease (1) from *hemochromatosis* or *bronzed diabetes,* (2) *arsenical pigmentations,* (3) *argyria,* (4) *pellagra,* (5) *Graves' disease,* (6) *cachexias* accompanying malaria, lues, tuberculosis or carcinoma, (7) certain *skin diseases* (vagabond's disease, xeroderma pigmentosum, melanosarcoma of the skin, chronic eczema).

### v. Pathogenesis of Addison's Disease

It is generally believed that Addison's disease is definitely dependent upon disease of the chromaffin system, especially that of the suprarenal glands, but cases are known in which, at autopsy, there was extreme disease of the suprarenal capsules though Addison's disease had not been present clinically, and there are other cases in which, clinically, Addison's disease has been pronounced, though no disease of the suprarenal glands could be found at autopsy. In one of the latter cases, Wiesel was able to demonstrate entire absence of certain other parts of the chromaffin system, and in one of the cases of severe tuberculosis of the suprarenal glands not accompanied by Addison's disease, he demonstrated excessive development of the chromaffin system outside the adrenals. It is Wiesel's belief that, for the development of Addison's disease, there must be disease of the chromaffin system and also of the suprarenal cortex (belonging to the interrenal system), but it is not necessary that the chromaffin system shall be diseased in its chief part (that is the suprarenal medulla), since destruction of portions of the chromaffin system outside the suprarenal glands will suffice. He believes that disease of the chromaffin system alone is insufficient to account for the phenomena of Addison's disease; participation of the suprarenal cortex in the disease is also necessary, especially to account for the most threatening symptoms of the disease. Studies of the lipoid granules of the suprarenal cortex and of the relations of the suprarenal cortex to the cholesterin-ester metabolism may later throw light upon this subject. Since the chromaffin system is under the dominion of the N. splanchnicus and the solar plexus, von Neusser believed that the site of the disease may be either in the chromaffin system itself or in the sympathetic nervous system innervating it.

One of the most interesting of the recent findings is the common association of hypoplasia of the chromaffin system with the so-called status thymicolymphaticus and the frequency of endocrinopathies of various sorts in persons presenting the status thymicolymphaticus is becoming well known. The merit of first calling attention to a persistent thymus in Addison's disease of the adult belongs to Star (1895), and the frequency of the relation has been established by Wiesel. It seems probable that the epinephrin secreted by the chromaffin cells exerts a depressive influence upon the thymus. If insufficient epinephrin be produced, the thymus does not undergo its normal involution.

It would seem that the pigmentation of Addison's disease may be due not to the chromaffin system directly, but to an abnormal disturbance of sympathetic

innervation, dependent possibly upon an auto-intoxication due to insufficiency of the suprarenal cortex, or more probably to a constitutional weakness of the sympathetic nervous system itself (Wiesel).

An attempt has been made by Wiesel to divide the symptoms of Addison's disease into two groups, (1) those due to *insufficiency of the chromaffin system proper* (adynamia, asthenia, arterial hypo-tension, stenocardia, mental depression, hypo-adrenalinemia, hypoglycemia), and (2) those due to *disturbance of the function of the suprarenal cortex* (gastro-intestinal symptoms, severe nervous symptoms, cachexia, exitus).

### vi. Prognosis in Addison's Disease

Addison's disease is nearly always progressive, ending fatally after several months or years. The average *duration* is two or three years. In very *acute cases* death may occur within three weeks after the first appearance of symptoms; in exceedingly *protracted cases,* with remissions and intermissions, a patient may live as long as thirteen years.

Thus far, no effective therapy has been devised other than purely symptomatic treatment and general upbuilding measures.

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### (*b*) *Over-function of the Chromaffin System*

### (*Hyperchromaffinopathy, Hyperepinephrinemia*)

Knowledge concerning functional over-activity of the chromaffin system is only at its beginning.

*Tumors* arising in the chromaffin tissues are rare (Küster, Schilder, Wiesel).

States of over-function of the chromaffin system are believed to occur in *contracted kidney,* in *general atherosclerosis* of the finer arteries, in *Graves' disease,* and sometimes, in *diabetes mellitus.* In most instances this over-activity appears to be called forth through nervous influences, either reflexly or through a state of over-excitability of the nerve centers.

In *chronic arterial hypertension,* hyperplasia of the chromaffin system has been observed (Wiesel). Attempts to demonstrate a hyperepinephrinemia in cases of arterial hypertension have yielded conflicting results, sometimes positive, sometimes negative. It seems certain that the blood serum sometimes contains constrictor substances other than epinephrin. In addition to the hyperplasia of the chromaffin system observed in chronic arterial hypertension, there are certain other points (polyuria, hyperglycemia, hyperglobulia) that, it has been thought, point to hyperchromaffinopathy.

Though it seems possible that over-activity of the chromaffin system is intimately related to sclerosis of the fine arterioles such as occurs in genuine contracted kidney, it does not seem likely that it has anything to do with the form of ordinary atherosclerosis of the large vessels that may be accompanied by hypertension. The relation of over-activity of the chromaffin system to diabetes mellitus and to the

premature atherosclerosis so often occurring in that disease, has begun to attract attention (Falta, Newburgh and Nobel).

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## (c) *Remarkable Sexual Syndromes Dependent Upon Hyperplasia, or Upon Tumors, of the Cortex of the Suprarenal Gland*

We are indebted to the French school (see Gallais' interesting monograph) for descriptions of certain very remarkable syndromes dependent upon *over-function of the interrenal system,* this over-function leading to changes in the sexual glands (gonads) and consequently to striking alterations in the secondary sexual characters. The French have grouped the clinical pictures under the designation *syndrôme génito-surrénale.* In the cases that have been studied, *tumors* starting from the cortex of the suprarenals have been found. Females are much more often affected than males, though a few males exhibit the syndrome.

This suprarenal genital syndrome assumes *three forms according* to the age in which the disease begins, (1) the congenital form (beginning before birth), (2) the early acquired form (beginning before adolescence), (3) the late form (beginning in adult life).

### i. The Congenital Form of Hyperinterrenopathy (Pseudohermaphroditismus)

Here belong certain females whose internal sexual organs resemble those of the normal female, but whose external genitals resemble the male type (enlarged clitoris, urethra of male type, prostate, slitlike vulva more or less closed, so as to resemble a scrotum).

In one such case, described by Marchand, there was extensive hyperplasia of the adrenal cortex and also a large interrenal body in the broad ligament. In another case, described by Meixner, the child seemed to be a male, but at autopsy the internal genitals were found to be of the female type, and two large interrenal bodies were present.

Recently I have had opportunity, through the courtesy of Dr. W. C. Quinby, of examining such a pseudohermaphrodite. The patient came to the Brady Clinic

Fig. 668.—Pseudohermaphrodite. Internal Genital Organs Female. External Genital Organs, General Configuration of the Body and Psyche Suggestive of the Male. (By Courtesy of Dr. W. C. Quinby.)

Fig. 669.—External Genitals in Pseudohermaphrodite of Preceding Figure. The Patient Was at First Supposed to Be a Male with Undescended Testicles, but Operation Revealed the Absence of Testicles and the Presence of the Internal Genitals of a Female. (By Courtesy of Dr. W. C. Quinby.)

(service of Prof. H. H. Young) for treatment of a supposed hypospadias. There were no testicles present and search was made for the undescended testicles, but on laparotomy the internal genitals of a female were found.

The opposite condition, in which the external appearance of the body and the external genitalia resemble those of a female, the internal genitalia being male, also occurs. The sex of the person is of course determined by the character of the internal genitals.

### ii. The Early Postnatal Form of Hyperinterrenopathy (Pubertas precox)

(*Pubertas precox*)

Here belong a part, at least, of the cases of *premature puberty.* Children appearing normal at birth and during the first few years of life, soon begin to show an *excessive fat development* (hips, buttocks, abdomen, mons veneris), an abnormally *rapid growth,* an *alteration in character* (excessive liveliness and unusual physical strength, which has led the French to designate them "Herculean infants"), and a *premature development of hair* on the external genitals, in the axillae, and, in males, on the face. The external genitals undergo the changes that correspond to those of *puberty* (enlargement of the penis or clitoris, increase in the size of the labia, closure of the vulva, turgescence, mammary gland development, menstruation; in boys, change of voice, with erections and pollutions).

These appearances, which may come as early as the fifth or sixth year of life or even earlier, are most startling. The condition is usually due to malignant new growth in the cortex of the suprarenals, ending fatally in one or two years, death being preceded by emaciation, cachexia, vomiting and diarrhea.

For full reference to the cases in the literature belonging to this group, the collective review of Neurath should be consulted.

That premature puberty may be due to a more benign cause sometimes is certain. In Charlotte, N. C., I saw a little girl about eight years old who had menstruated since infancy; she looked sexually mature, and seemed a healthy child otherwise. Recently, I saw, in Prof. H. A. Kelly's clinic, a girl of 7 years with pubertas precox associated with a large ovarian tumor.

### iii. The Late, or Adult, Form of Postnatal Hyperinterrenopathy

(*Suprarenal Virilismus, Hirsutismus*)

When the interrenal tumor develops after the ordinary age of puberty, that is *after* the secondary sexual characters have already developed normally, another clinical picture may appear, namely, *virilismus* or *hirsutismus.*

Females between 15 and 20 are most often affected, though the condition may set in at any time before the menopause. At the beginning, the patient complains of disturbances of menstruation (irregularity, amenorrhea), nausea and vomiting, and obesity, though it is often stated that she is unusually well and strong physically, the muscular power being excessively developed ("masculine women") and making the girl capable of performing physical tasks of which ordinary women are incapable. This *hypersthenia* of the suprarenal genital syndrome is in marked contrast with the asthenia of Addison's disease. A curious *mental change* may

also appear (egotism, overbearing tendency, irritability), a kind of *mental hypersthenia.* Some of the patients show an abnormally strong sexual excitability.

The *hair* on the body undergoes a remarkable change. Thus women, when affected by the disease, grow moustaches or beards; instead of the upper transverse limitation of the crines pubis characteristic of woman, the triangular form of crines characteristic of the male appears. Long hairs may grow on the abdomen, the chest, the shoulders, the back and the extremities; hence the name *hirsutismus* given by Guthrie and Emery (1907).

Aside from the hypertrophy of the clitoris and the change in the crines pubis, the external genitalia remain normal. General pigmentation of the skin has been noticed in some cases; in others, local patches of dirty gray pigmentation have appeared.

The changes above described characterize the early stage of the disease. After a few months, however, more serious symptoms set in (emaciation, adynamia, melancholia, frigidity), not unlike those of Addison's disease. Albuminuria appears, the blood pressure falls, and drawing and shooting pains in the trunk are complained of. Often, at this stage, a retroperitoneal tumor becomes palpable, and death soon follows. Tubal pregnancy seems to have been common in connection with interrenal tumors.

The *diagnosis* of interrenal tumor (hypernephroma) is easy in typical cases when a retroperitoneal tumor is demonstrable. The tumor may be very large. In one case I saw, the mass reminded me at first of a large leukemic spleen. If no tumor be palpable, a probability-diagnosis may be made from the other symptoms, or from signs pointing to metastases in the lungs, the occipital bone, or the clavicles. Paroxysmal pains and paresthesias in the domain of distribution of the lumbar plexus, with fever, and hematuria in the absence of nephrolithiasis are suggestive.

In the *differential diagnosis,* one must distinguish the condition (1) from *dystrophia adiposogenitalis due to hypophyseal tumor* (congenital hypoplasia, loss of secondary sexual hair, x-ray of sella turcica), and (2) from *tumor of the corpus pineale* (choked disk, x-ray, signs of increased intracranial pressure).

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# G. Diseases of the Thymus

## 1. Introduction

Formerly recognized as a part of the lymphatic apparatus, clinicians have recently come to recognize that the thymus belongs also to the great group of glands of internal secretion, and is therefore to be viewed as one of the hormonopoietic organs.

The *functions* of the thymus are as yet but poorly understood. If the thymus be *extirpated* in very young animals serious symptoms develop. Thus, in dogs, thymectomized a few days after birth, the skin soon becomes spongy and soft, the growth of the animal is retarded, especially the longitudinal growth of the extremities, the bones soften and bend, ossification is slowed, there is little or no callus-building after fracture, lime-deficit develops, and dentition is slowed. The animals put on fat at first, but, later, become cachectic, in spite of a good appetite.

Muscular tremor develops; the animals become anemic and sluggish; and, finally, they enter a comatose state before death. If thymus gland be fed to them, or if thymus extracts be injected, they do not improve. The studies of Howland and his associates, however, make the validity of the preceding observations seem doubtful.

Thymectomy in older animals causes only temporary symptoms, unless the spleen be simultaneously removed, in which event the animals develop serious symptoms and die.

Normally, in human beings, at puberty, the thymus ceases to be as active as formerly; and its tissue gradually atrophies, becoming in large part replaced by adipose tissue, though some thymus tissue remains throughout life.

If young animals be castrated, the normal involution of the thymus is markedly delayed. In human eunuchs, the thymus is known to persist. Excessive sexual activity in early life is said to accelerate the involution of the thymus.

Clinicians are now attempting to set up syndromes dependent upon states of *under-function* and states of *over-function* of the thymus (*hypothymismus, hyperthymismus*).

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## 2. States of Under-function of the Thymus Gland (Hypothymismus and Athymismus)

Total extirpation of the thymus has been performed on account of tracheal stenosis in young children (Rehn), but we are not told what the results have been.

Congenital defect of the thymus has been reported (von Sury), but the condition can scarcely be recognized during life. Now that the thymus is being extirpated in certain cases of Graves' disease where the thyroid is small, it seems probable that our knowledge of hypothymismus may rapidly increase.

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## 3. States of Over-function of the Thymus Gland

*(Hyperthymismus, Status thymicolymphaticus, Asthma thymicus, Mors thymica)*

### (a) *Conception of Status thymicus*

Since Kopp called attention in 1855 to instances of *sudden death in childhood* following cyanosis and stridor, in which, at autopsy, nothing abnormal except a *hyperplastic thymus* could be found, clinicians have paid much attention to hyperplasia of the thymus and to faulty involution

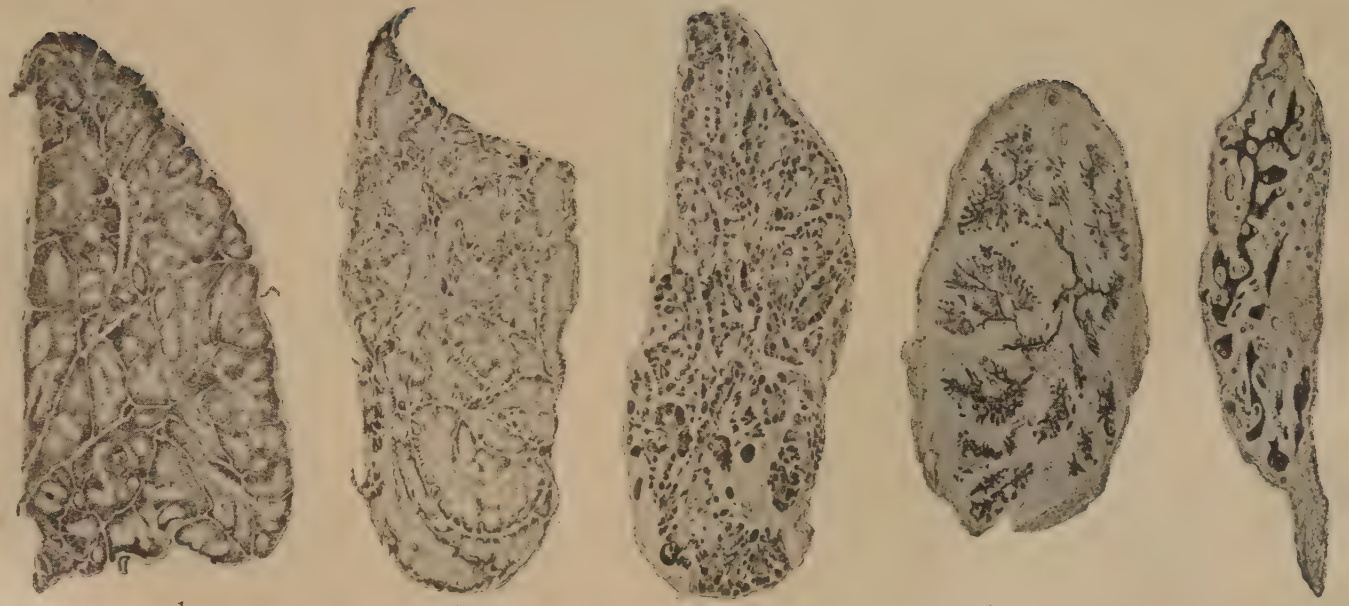


Fig. 670.—Sections of Human Thymus at Various Ages, Enlarged About 3 x. 1. New-born. Thymus—wt. 15 gm. 2. Child æt. 7 Years. Thymus—wt. 35 gm. 3. Boy, æt. 17 Years. Thymus—wt. 35.2 gm. 4. Boy, æt. 17 Years. Dead After 24 Days' Illness with Empyema. Moderate Accidental Involution. Thymus—wt. 8.8 gm. 5. Boy, æt. 17 Years. Dead of Tuberculosis. High Grade of Accidental Involution. Thymus—wt. 1.65 gm. (After Hammar in A. Biedl's "Innere Sekretion," published by Urban & Schwarzenberg, Berlin.)

thereof, sometimes, though inadequately, designated as *persistence* or *revivescence of the thymus.*

The fundamental studies of A. Paltauf in 1889 established the frequent combination of hyperplasia of the thymus with status lymphaticus and with aplasia of the cardiovascular system, and it was he who called attention to the necessity of considering causes other than mechanical in the sudden deaths (*mors thymica*) among such patients. Paltauf believed that the exitus depends rather upon some vegetative disturbance connected with what he designated the *lymphatic-chlorotic constitution.*

Fig. 671.—Very Large Thymus from a Boy Dying Four Hours after Birth. The Thymus Filled the Larger Part of Both Sides of the Thorax. (After H. Klose, "Chirurg. d. Thymusdrüse, published by F. Enke, Stuttgart.)

As the condition became more carefully studied, it was found that, in certain families, a number of sudden deaths from this cause occur (Hedinger). For a time, it was thought that an abnormally large thymus was always accompanied by a status lymphaticus, but it is now believed that a *status thymicus* can occur independently of a status lymphaticus, though the combination—*status thymicolymphaticus*—is very common.

In status lymphaticus, there is always *hypoplasia of the chromaffin system* (Wiesel and Hedinger); indeed the status lymphaticus may apparently be secondary to the hypochromaffinopathy. In pure hyperplasia of the thymus (status thymicus), the chromaffin system may sometimes be entirely normal (Hedinger). In thymic death of the new-born, it is asserted by some that the chromaffin system is well developed, and that it is only later on, when the status lymphaticus develops, that hypoplasia of the chromaffin system is found (von Sury). The whole subject is at present in a state of uncertainty and we must await further investigation before a definite decision can be reached. Should the current view be true, cases of pure hyperplasia of the thymus without status lymphaticus should not exhibit a lymphocytosis, for in pure status thymicus, the hyperplasia is said to concern chiefly the epithelial part of the organ (Hassall's corpuscles and the cells on the reticulum), while in status lymphaticus it is the small mononuclear elements that are markedly increased in numbers.

In cases of sudden death, great care should be taken before asserting that the thymus is abnormally large. The thymus varies greatly in *size* under physiological circumstances. Hammar has attempted to determine the normal weight, at different ages, so as to make reliable comparisons possible, but unless a histological study be made and the relative amounts of lymphatic tissue, epithelial tissue, fat and connective tissue determined, the results may be very misleading.

### (*b*) *Symptoms of Status thymicolymphaticus*

The *status thymicolymphaticus* is a constitutional anomaly (Paltauf, Hart, Bartel, von Neusser, Wiesel). There are many transitions from it to the *hypoplastic constitution* of Bartel and to the *eunuchoid type* of Tandler and Grosz.

In the United States, we are much indebted to Dr. Haven Emerson, of New York, for his careful descriptions of status thymicolymphaticus. The *external appearance* of patients is often characteristic. They may be either abnormally *tall* or abnormally *short,* and they usually have long arms and legs. The *head* may be small or large, and anomalies of the *skull* are common.

**Males** often exhibit a feminine configuration (*typus femininus*) of their extremities. Thus they may exhibit rounded arms and thighs, gynecomastia, broad hips, excessive development of the middle incisor teeth, low position of the umbilicus approaching the symphysis pubis, delicate clavicles, over-extensibility of the elbow, and the feminine relation of upper length to lower length of the body.

The *skin* looks pasty. The distribution of the *hairs* is often heterosexual. Thus, in males, the beard is feebly developed, the hair over the sternum is scanty or absent, the same being true of the hair on the abdomen, the extremities, and the perineum. The hirci are also scanty; the crines pubis are limited by a horizontal line above and the hairs are relatively scanty, as in woman. Fine down may also be present on the cheeks, as in woman.

In **females,** the distribution of the *hairs* may assume a masculine type, coarse hairs being abundant on the trunk and extremities. The crines pubis may extend as a triangle up toward the umbilicus, as in the male, and hairs may appear on the perineum and around the anus. Occasionally, the hair of the head is abundant, while the crines pubis and the hirci are scanty.

The distribution of the *fat* is often abnormal, males having a distribution like that of females and *vice versa.* The whole *skeleton* may be either longer or shorter than normal. The *epiphyseal lines* may remain open to a late date.

The *thyroid* is usually, though not always, enlarged. The *lymphatic apparatus* of the body is usually hypertrophied, though thymus hyperplasia may exist without hyperplasia of the lymphatic apparatus. It would seem, however, that the status thymicolymphaticus of Paltauf may be taken as a principal type from which the status thymicus, the status lymphaticus, the infantile arthritismus (Comby), the exudative diathesis (Czerny), the so-called lymphatismus (Heubner), and the lipomatous type (Kryloff) are deviations.

In outspoken cases of status thymicolymphaticus, there is always hyperplasia of the lymphatic system (Virchow, Ortner). The intestine is often abnormally long. Congenital anomalies of the kidney are not uncommon. Hypoplasia of the suprarenals and of the chromaffin system is usually present (Wiesel).

Genital anomalies are common; thus, in the male, the *external genitalia* may be small, and *cryptorchismus* is common. In some cases, the scrotum is absent. In the female, the *vagina* may be narrow, the *uterus* infantile, the *fallopian tubes* long and twisted and the *ovaries* large and smooth.

Hypertrophy of the *brain* may co-exist and *juvenile osteomalacia* may be met with.

Thymus hyperplasia is never accompanied by all the conditions mentioned, a variable number being present in each case.

In *children,* especially, it may not be possible to determine the presence or absence of many of the anatomical peculiarities mentioned, but the clinician's attention will be drawn to the condition by the so-called *pasty habitus,* a combination of (1) pallor of the skin, (2) excessive watery, subcutaneous adipose tissue, and (3) a relaxed muscular system. Among the clinical manifestations associated with status thymicolymphaticus may be mentioned paroxysmal palpitation of the heart, dyspnea, cyanosis, insomnia, rapid changes in body weight, and variable temperature.

Fig. 672.—Showing Pressure of the Thymus on the Trachea when the Head Is Bent Backwards. (After Ehrhardt-Beneke in H. Klose, "Chirurg. d. Thymusdrüse," published by F. Enke, Stuttgart.)

The sudden death of young children and even of adults in status thymicolymphaticus—the so-called **mors thymica**—has been variously explained. Many of the patients have died suddenly while taking a bath, others under punishment, adults occasionally in coitus, after an injection of antitoxin, or during narcosis. In some of these cases, the death may be mechanically caused through *compression of the trachea* by the enlarged thymus. A child put to sleep upon its face may die from suffocation, but many of the deaths are probably not mechanical in origin, but due to *heart shock* or to *infection,* to which the thymus-hyperplasia seems to predispose. Many of the sudden deaths in eczematous children are thus to be explained.

Undoubtedly, an enlarged thymus can cause symptoms of stenosis of the trachea **(tracheostenosis thymica).** Many young children have attacks in which they stop breathing, become cyanotic, and lose consciousness for a moment or two and then recover. A child may die in such an attack, but this is unusual. It is not uncommon to observe attacks in several children of the same family. Anything that causes *overextension of the head* may bring on an attack; similarly, anything that

causes *venous stasis* in the thymus gland may cause an attack (coughing, crying, infection, intoxication, narcosis). In some children, signs of chronic tracheostenosis are visible—the so-called *stridor thymicus infantum* of Hochsinger. They exhibit noisy breathing, especially at the end of inspiration, or when excited. The children are a little cyanotic and polypneic.

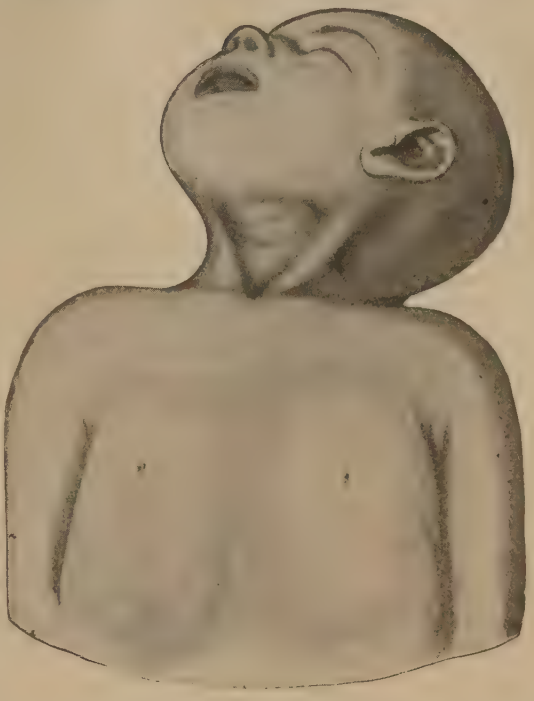

Fig. 673.—Asphyxia in Hyperplasia of the Thymus. Sinking in of the Anterior Neck Region, Contraction of the Auxiliary Muscles of Respiration, Drawing in of the Lower Thorax on Inspiration. (After H. Klose, "Chirurg. d. Thymusdrüse," published by F. Enke, Stuttgart.)

The *attacks of suffocation* above referred to are most common in infants between the 6th and the 12th month of life. They are usually preceded by restlessness. In the attack itself, the child throws its head backward and attempts to inspire, the eyes turn upward, the pupils dilate, the lips and tongue become blue and swollen, the veins of the neck are engorged, the hands are clenched, the body is bent backward, a few convulsive movements appear in the face, and the child becomes unconscious. The lividity soon gives way to pallor. If the attack is fatal, death occurs in a minute or two. Many children recover, lying limp and pallid for a few minutes, or even for an hour or two, and then become normal again.

The recognition of **enlargement of the thymus** by physical signs is not always easy. Occasionally, on expiration, the upper end of the thymus can be seen rising in the jugulum and can be palpated there. If there be absolute dullness behind the manubrium sterni, extending to the left beyond the sternal margin, and fusing with the heart dullness, it is an important sign of enlargement of the thymus (Marfan and Klose). Of course aneurism of the aorta or substernal struma could give a similar dullness. Boggs has emphasized the movable dullness in the thymus region (2nd left intercostal space) on flexion and on over-extension of the head.

On *röntgenoscopic examination,* an enlarged thymus can be seen to

descend on inspiration and to rise on expiration (Rehn). In *röntgenograms*, a normal thymus is seen as a median shadow sitting on top of the heart shadow like the narrow neck of a flask. If the thymus be hypertrophic, the neck of the flask is enlarged (Hochsinger).

The diagnosis of *stenosis of the trachea* due to compression from enlargement of the thymus must often be made in the absence of physical signs and of positive x-ray findings. Because of the danger from it, and on account of the desirability in some cases of surgical interference, the condition should not be overlooked.

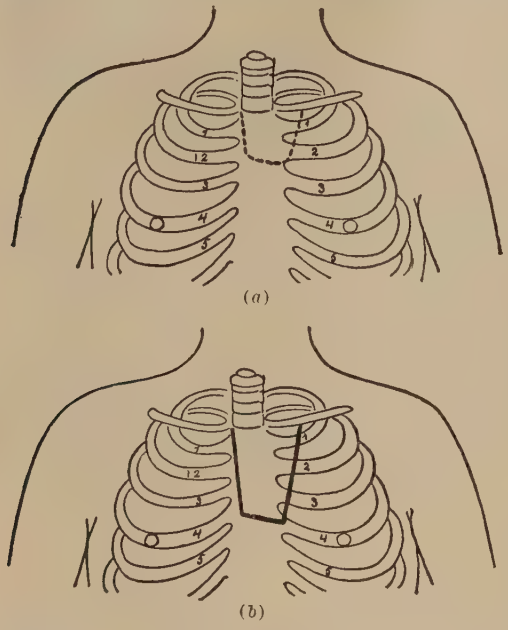

Fig. 674.—(*a*) Normal Thymus Dullness. (After Basch, Marfan and Klose.) (*b*) Enlarged Thymus Dullness. (After Marfan and Klose in H. Klose, "Chirurg. d. Thymusdrüse," published by F. Enke, Stuttgart.)

An enlarged thymus may cause *dysphagia* through compression of the esophagus (*thymogenous stenosis of the esophagus*). It may cause compression of the N. vagus; or it may lead to compression of the large vessels and of the atria of the heart in the upper thorax.

Though the thymus does not seem to be one of the main hematopoietic organs, actively participating in blood formation, it is probable that the internal secretion of the thymus may exert an important *influence upon the blood-building apparatus*. Thus, experimental thymectomy is followed by a progressive diminution in the number of the lymphocytes; intravenous injections of thymus juice or implantation of thymus gland will, on the other hand, cause an outspoken **lymphocytosis.**

The high lymphocyte count in children as compared with the count in adults may depend upon the fact that the thymus is larger and more active in early life than later. In leukemic lymphadenosis, there is always a marked proliferation of the thymus, whereas in leukemic myelosis, the thymus gland is not involved or, if at all, only slightly.

In children with hyperplastic thymus there may be an excessive lymphocytosis (80 per cent to 85 per cent), while children with insufficient thymus may show a lymphocytopenia (reduction to 9 per cent or to 10 per cent).

After operative removal of the thymus in human beings the lymphocytes quickly diminish in number. A high percentage of lymphocytes in Basedow's disease suggests hyperplasia of the thymus (*Basedow-thymus*).

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# H. Diseases of the Sex Glands or Gonads

(*The Gonadopathies*)

## 1. Introduction

Here we shall deal only with the diseases of the sex glands or gonads depending upon disturbances of their internal secretions (*endocrine functions*); the diseases of their specific generative parts are discussed in Part X.

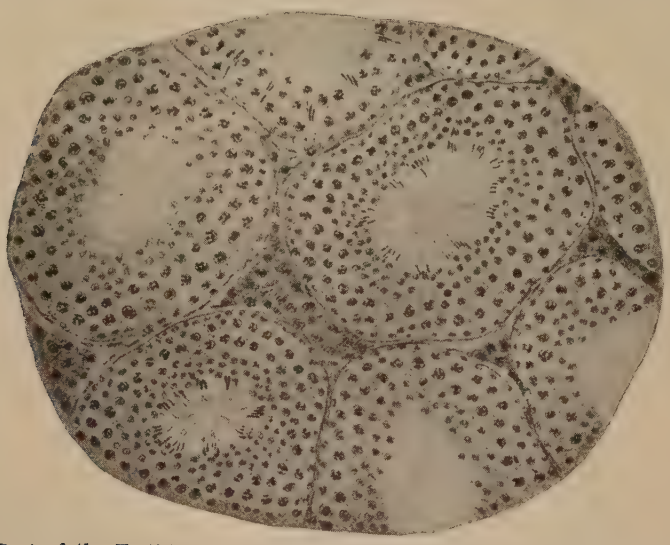

Fig. 675.—Part of the Testicle of an Adult Rabbit. Advanced Spermatogenesis and Scanty Interstitial Cells. Magnification x 180. (After Bouin et Ancel in A. Biedl's "Innere Sekretion," published by Urban & Schwarzenberg, Berlin.)

In the **male**, the endocrine part of the testicle consists of the so-

called *interstitial cells of Leydig.* These are aggregations of epithelioid cells containing both acidophile and basophile granules, the cells resembling somewhat those of the suprarenal cortex, and being, like the latter, mesoblastic in origin.

In the **female,** it is the interstitial cells of the ovary and, perhaps, the cells of the corpora lutea that are responsible for the endocrine function.

There seems to be no doubt that the secretion from these interstitial cells of the gonads is important for the development of the **secondary sexual characters** in both the male and the female, at puberty. Before puberty, the bodies of boys and girls resemble one another closely; in both

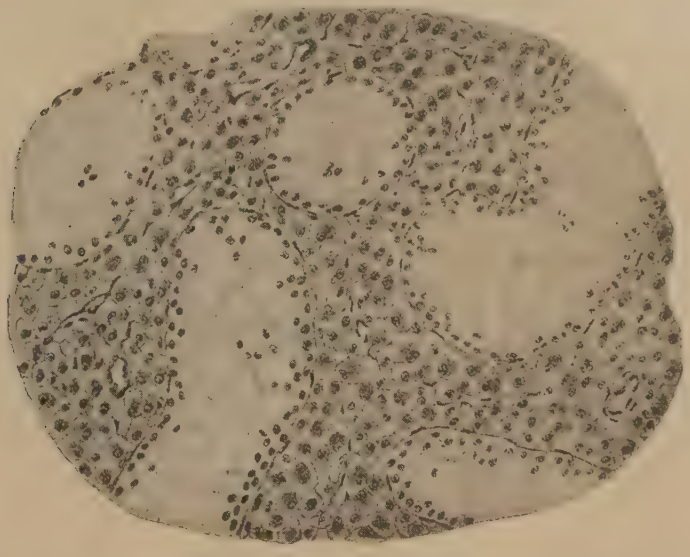

Fig. 676.—Part of the Testicle of a Rabbit Some Months After Unilateral Vasectomy and Simultaneous Extirpation of the Testicle on the Other Side. No Spermatogenesis; Only the Syncytium of Sertoli Appears in the Seminiferous Tubules. The Interstitial Tissue Is Markedly Proliferated. (After Bouin et Ancel in A. Biedl's "Innere Sekretion," published by Urban & Schwarzenberg, Berlin.)

sexes, the type is infantile, but at puberty, along with the marked hypertrophy of the gonads, those changes take place in each sex that characterize the masculine and the feminine type respectively.

Thus the growth of the whole body is very rapid at **puberty.** In the *boy,* the larynx enlarges, the voice changes, and the beard and the moustache begin to grow. In *girls,* the breasts enlarge, the pelvis expands, and fat is deposited about the hips. In *both sexes,* hairs appear in the axillae —the so-called hirci, and above the symphysis pubis—the so-called crines pubis. The hair above the pubis in the male assumes a triangular dispo-

sition, the apex of the triangle extending towards the umbilicus; in the female, the hair on the mons veneris is limited above by a horizontal line.

Though the endocrine functions and the generative functions of the sex glands possess a certain independence of one another, these functions are also definitely related to one another; they reciprocally influence one another. In *pregnancy,* the generative function is for the time held up. It has been assumed by some that the endocrine function is also inhibited by pregnancy, but Falta and others dispute this view, especially as the interstitial cells of the ovary proliferate markedly in the late months of pregnancy, and because during pregnancy, as in the premenstrual period, signs of increased vitality of the whole organism are observable (thyroid enlargement, hypertrophy of suprarenal cortex, and signs of increased function of the chromaffin system, including epinephrin-glycosuria, arterial hypertension, slight hyperglobulia, elevation of the body temperature,

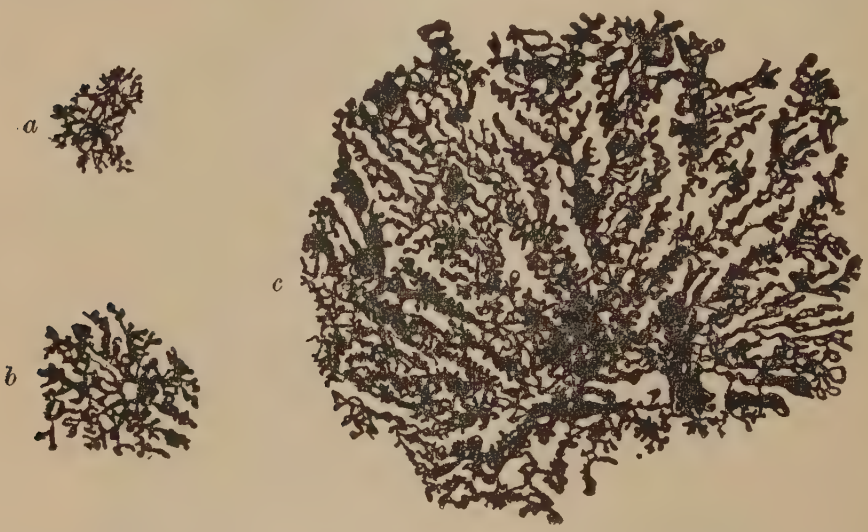


Fig. 677.—Breast of a Rabbit. (*a*) Virgin Animal; (*b*) Five Days After First Fecundation; (*c*) Nine Days After Fecundation. (After Starling in A. Biedl's "Innere Sekretion," published by Urban & Schwarzenberg, Berlin.)

slight neutrophilic leukocytosis, and acceleration of the coagulation of the blood). Moreover, during pregnancy we see also hypertrophy of the nasal conchae, enlargement of the breasts, unusual pigmentations, unusual development of hair, osteophyte formation, and slight enlargement of the acra; some of these changes are presumably due to an increased function of the glandular portion of the hypophysis cerebri. It is the activity of the follicular apparatus of the ovary, alone, that stops during pregnancy and leads to the lipoidemia of pregnancy similar to that which occurs at the climacteric or after spaying (Neumann and Hermann). After the birth of the child, all of the above signs disappear, the whole vegetative nervous system becomes less excitable, the pulse becomes slower, and the blood shows a leukopenia with mononucleosis.

Everyone is familiar with the increased irritability of women just preceding *menstruation.* There is some evidence that all the metabolic processes are accel-

erated in the pre-menstrual period. In women with psychopathic tendency, psychotic symptoms often appear during the puerperium, or after menstruation has set in.

Clinicians are beginning to recognize states of the body depending upon *over-function* and other states depending upon *under-function* of the endocrine part of the sexual glands. These are known respectively as *hypergenitalism* and *hypogenitalism.*

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## 2. States of Over-function of the Gonads

(*Hypergenitalism*)

### (*a*) *Primary and Secondary Hypergenitalism*

When discussing diseases of the epiphysis cerebri and diseases of the interrenal system, examples of hypergenitalismus were given (*q. v.*), but in addition to this hypergenitalism secondary to diseases of other endocrine glands, there are cases that at present must be regarded as primary disturbances in the gonads that lead to hypergenitalism. In some of these cases malignant tumors of the ovaries or testicles have been found. In other cases simple hypertrophy of the sex glands was observable. Falta calls attention to the coincidence of hydrocephalus with hypergenitalismus in two of the cases reported.

### (*b*) *Symptoms of Hypergenitalism*

In the collective review by Neurath of 43 cases of premature sexual development in boys, the clinical signs include (1) premature and excessive development of the external genitals and of the secondary sexual characters, (2) premature change of voice, and (3) excessive development of the body as a whole.

In male children who manifest such a **pubertas precox**, the sexual impulse may develop in early childhood with erections and ejaculations. Many of these boys show a partial gigantism, but owing to the tendency to early closure of the epiphyseal lines in hypergenitalism, the height may finally be less than normal (dwarfism), despite the fact that the boy has been relatively tall in his early childhood. The mentality may remain infantile, though it is markedly modified by the premature sexual development.

A remarkable instance is the case reported by Sacchi in which the signs of hypergenitalism began at the 5th year of life in association with a tumor of the left testicle. This boy was operated on in his 9th year, the tumor being removed. A month later, the hairs of the beard and of the extremities, which had developed prematurely, fell out, though the crines pubis persisted; the external genitals grew smaller, the erections and pollutions ceased, and the voice, which had changed, again became infantile.

Many instances of hypergenitalism in the female are to be found in the bibliography, described as precocious menstruation or **menstruatio precox**. No less than 83 cases have been collected by Neurath. As a rule, the change takes places in the second year of life. The external genitals begin to enlarge and grow faster than the internal genitals, the

breasts develop and the hirci and the crines pubis appear abnormally early. The skeleton grows too rapidly. Both sets of teeth come prematurely. The ossification centers appear more early than normal, and the epiphyseal lines are closed at an early date.

In a case described by Klein, a little girl began to menstruate at two and a half years, her vulva being the size of that of a fourteen-year-old girl. In von Haller's case menstruation appeared at two years. She became pregnant at eight, and, shortly after, the excessive growth of the skeleton ceased. She grew to be a woman and lived to be seventy-five years old. In a patient described by Riedl, menstruation appeared in the 6th year, when the uterus was as large as that of a seventeen-year-old girl. After removal of a sarcoma of the ovary, menstruation ceased. Since becoming interested in these cases, I have had several reports from American physicians of similar observations, and in Charlotte, N. C., I was given the opportunity of carefully examining a girl of eight who had begun to menstruate in infancy.

Dr. Margaret Mackellar, of Neemuch, Central India, has recently written me of a child under her observation that menstruated from birth on!

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## 3. States of Under-function of the Gonads

(*Agenitalism, Hypogenitalism*)

At least three groups of cases are distinguishable in males: (1) true eunuchs, or persons in whom the sex glands have been destroyed by operation, (2) eunuchoids, or persons in whom there is insufficiency of the gonads at an early period of life, and (3) late eunuchoids, in whom the gonads have been sufficient up to the period of full development, but later

on have become insufficient. In females, we have the opportunity of studying agenitalism after double oöphorectomy; and at the natural menopause, symptoms of hypogenitalism often develop.

### (*a*) *True Eunuchs*

(*Agenitalism*)

**Castration.**—In ancient times, *castration* of males was a common practice. It is not so very long since certain males in Italy were castrated for "musical purposes." Even today, there is a religious sect in Russia and in Roumania—the so-called Skopzi—among whom castration is practised as a religious rite. The latter have recently been made the subject of a careful study by Tandler and Grosz (see references).

Concerning the spaying of females in early life, we have but little information. In the gynecological literature, there are some studies of the symptoms of the "artificial menopause" that follows double oöphorectomy. When the latter operation first became popular at the end of the last century, many young women suffered from the wave of surgical enthusiasm that spread over the country. Unfortunately, only a meager literature regarding the effects of the operation in early life exists.

**Symptoms.**—The symptoms in the male vary greatly according as the castration is done before or after puberty. When castration is done early, the penis, the prostate and the seminal vesicles remain small, the sexual impulse does not develop, and the person never has erections. If the operation be done in later life, there is less change in the penis, though the prostate atrophies markedly, a fact that led surgeons at one time to perform castration to relieve prostatic hypertrophy. In these cases, however, sexual impulse need not change, at any rate for a long time; coitus may still be practised, with ejaculation of prostatic secretion.

That the *psyche of eunuchs* differs materially from that of normal men, there can be no doubt. Eunuchs lack the courage, and the capacity for passion and for struggle that is normal in man. Some of them, however, attain to high intellectual powers. It has even been asserted that eunuchs possess superior artistic ability, but this is doubted by others. Castrated animals (ox, horse, capon) show alterations of the emotions and of the will similar to those observed in human beings.

The average *height* of eunuchs exceeds the normal. This has been observed among most races, though the height of Chinese eunuchs is not so striking as that of eunuchs of other races. Among the Skopzi, studied by Tandler and Grosz, *two principal types* are distinguishable. In one, the eunuchs are tall and relatively thin; in the other they are strikingly fat and pudgy looking, having broad hips and accumulations of fat in the

buttocks and breasts and over the trochanters and the crests of the ilia. Even the thin eunuchs (first type) exhibit unusual fat deposits (lower abdomen, mons veneris, buttocks). In both instances the distribution of the fat is practically the same as in the dystrophia adiposogenitalis of hypophyseal origin (*q. v.*). On account of the long legs, the lower half of the body is longer than the upper half. These eunuchs have abnormally long arms also, and in one instance when the arms were outstretched the distance from finger-tips to finger-tips measured 204 cm.

Fig. 678.—Man, aet. 24, Castrated at 5 Years. Note the Disproportionate Length of the Extremities. Total Length, 184 cm.; Span, 204 cm.; Lower Length, 108 cm. (After J. Tandler u. S. Grosz, "Die biol. Grundlag. d. sekund. Geschlechtschar.," published by J. Springer, Berlin.)

The head of the eunuch is small, the back of the head is flattened, the upper edge of the orbit is prominent, and the sella turcica is large. The pelvis is broad. Genu valgum is common. The epiphyses remain long ununited.

The pale or sallow skin is often thrown up into folds; it looks waxy, and contains less pigment than normal. A eunuch may have a good head of hair, but the beard is absent, except for a slight lanugolike growth on the upper lip. In advanced life a few hairs may appear on the face, similar in distribution to that seen in old women. The hirci are scanty. The crines pubis are feebly developed and are feminine in type (horizontal limit above), and hairs do not develop in the normal way upon the perineum, the trunk and the extremities.

The neck remains infantile, not undergoing the normal modelling at puberty. The larynx remains small, accounting for the high-pitched voice (retention of the childlike soprano). The thyroid is always small.

Eunuchs are usually dull looking persons, partly owing to the psychic anomaly, partly to the sleepy appearance given to the face by little masses of fat in the lateral half of the upper eyelids. The general attitude of the eunuch is relaxed, the gait heavy and clumsy.

Fig. 679.—Man, aet. 35, Castrated when 8 Years Old. Note the Beardless, Fat Face, with Mass of Fat in the Upper Eyelid. (After J. Tandler u. S. Grosz, "Die biol. Grundlag. d. sekund. Geschlechtscharakter.," published by J. Springer, Berlin.)

Concerning the results of early *spaying of females*, our information is less accurate. According to Roberts, who has studied the condition in India, the girls grow tall, the genitals remain infantile, the secondary sex characters and the breasts fail to develop.

In double oöphorectomy after puberty, menstruation ceases and the uterus and the vagina atrophy. The skin loses much of its pigment and the women tend to become obese. In animals that have been spayed, the total (caloric) metabolism may be reduced as much as 20 per cent (Loewy and Richter), but it is said to become normal again on feeding ovarian substance.

Following double oöphorectomy, the acute loss of the gonads gives rise to a set of symptoms known as those of the *artificial menopause;* these symptoms include various signs of excitation in the autonomic nervous system, pains in the extremities, hot flushes, feelings of anxiety and apprehension, fainting spells, hot and cold sensations, digestive disturbances, etc.

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### (*b*) *The Eunuchoids*

(*Hypogenitalism, Eunuchoidism*)

**Nature.**—The conception of *eunuchoid* persons, that is to say, persons with hypoplastic sex organs and bodily configuration similar to that of eunuchs though eunuchoids have not been castrated, we owe to the English school (J. Griffiths, 1894; W. L. H. Duckworth, 1907). When the

Fig. 680.—Eunuchoid, aet. 51. Fat Accumulations Over the Lower Abdomen and Iliac Crests; Genital Hypoplasia. (After J. Tandler u. S. Grosz, "Die biol. Grundlag. d. sekund. Geschlechtschar.," published by J. Springer, Berlin.)

Fig. 681.—Eunuchoid, aet. 26. Fat Accumulations in the Breasts and Lower Abdomen. (After J. Tandler u. S. Grosz, "Die biol. Grundlag. d. sekund. Geschlechtschar.," published by J. Springer, Berlin.)

condition is recognizable at puberty, it is known as *early eunuchoidism,* but when it appears after puberty, during the active period of sexual life (before the climacteric period), it is known as *late eunuchoidism* (Falta).

Though the eunuchoid condition depends mainly upon a hypogenitalismus, the other glands of internal secretion are simultaneously involved to a greater or less extent, so that some authors include eunuchoidism among the so-called multiglandular syndromes. In the bibliography, instances of eunuchoidism will be found among cases designated under various cap-

tions (*dysgenitalismus, dystrophia adiposogenitalis, infantilism with gigantism, obesity of genital origin, infantilisme tardif* or *reversif, geroderma distrofico*, etc.).

Fig. 682.—Eunuchoid Infantilism with Acromegaly. Age 45. (Med. Service, J. H. H.)

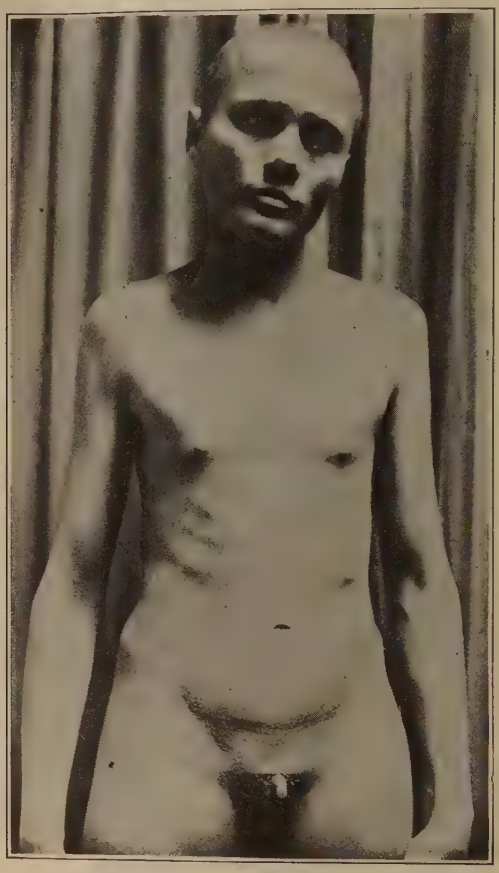
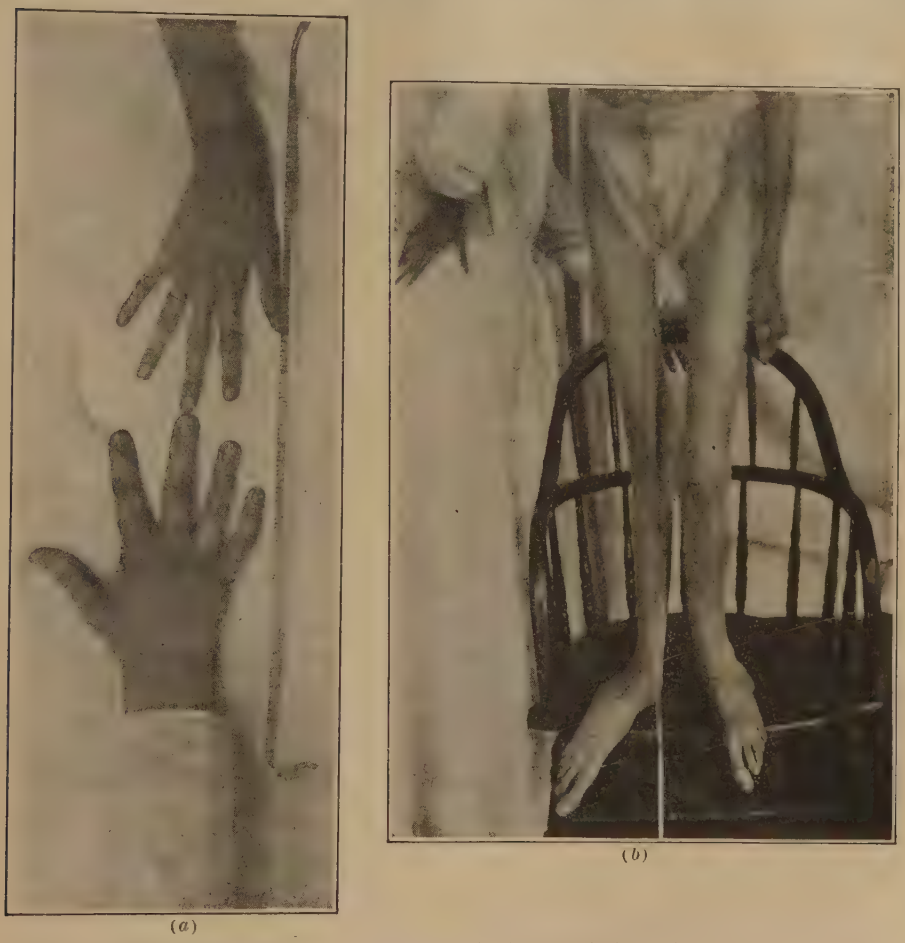


Fig. 683.—Eunuchoid. Med. Service, J. H. H.)

**Symptoms.**—The symptoms observable in eunuchoids resemble those met with in eunuchs on the one hand (though the patients have not been castrated or spayed), and those of persons suffering from hypophyseal dystrophia adiposogenitalis, on the other (though disturbances of vision and changes in the sella turcica are not demonstrable). Most of the patients are taller than normal. Falta believes that we have, in these cases, to deal with a *primary disturbance of the gonads* (primary hypogenitalism); others maintain that we have to deal with a *multiglandular syndrome,* not with a disease necessarily limited to the sex-glands.

Two types, similar to the two types of eunuchs, are described: (1) the *tall eunuchoid,* and (2) the *fat eunuchoid.* Even the fat eunuchoid seems

never to be below normal height. The skeletal form, the distribution of fat, and the defective development of the secondary sexual characters resemble those of eunuchs. Psychically, the patients are quiet, taciturn, and



(*a*) (*b*)

Fig. 684.—Hypogenitalismus. *a*, Gracile Hand in Hypogenitalism Contrasted with Normal Hand. *b*, Long Narrow Feet in Patient with Hypogenitalism and Infantilism. (Med. Service, J. H. H.)

lack independence (Tandler and Grosz). The genitals are hypoplastic. In males, one testicle may be undescended (cryptorchism).

In both sexes, those affected are sterile and usually lacking in sexual desire. In some cases the development may have been normal for a time, the symptoms later setting in suddenly. In some cases, the disturbances may be temporary, normal development going on later.

According to Falta, cases of *dystrophia adiposogenitalis* are divisible, clinically, into two groups: (a) the *hypophyseal group*, depending upon primary insufficiency of the glandular hypophysis, and (b) the *cunuchoid*

*group,* depending upon primary hypoplasia of the gonads. When the patients are as tall or taller than normal, hypogenitalism is more probable than hypopituitarism.

The changes in the skin and hair in eunuchoids are very interesting. The skin of the face is pale and delicate, but innumerable wrinkles and folds soon appear; later on, the color becomes sallow or gray. About the lower jaw and chin, small, horseshoe-shaped wrinkles appear, and linear wrinkles radiate from the angles of the mouth. The patients look prematurely old.

When the disease develops early, the secondary sexual hair fails to develop at all or, at least, is scanty. In older persons, the hair falls out. The total change in the hair closely resembles that described as *oligotrichosis lanuginis terminalis* (Friedenthal).

In the *late eunuchoidism* of Falta, the organism has undergone full development with normal function of the gonads, but, later on, regressive changes have involved the external genitalia, the secondary sex characters, and the psyche, owing to disease of the sex glands and diminution of their endocrine functions. Traumatism, syphilis, or gonorrhea have been thought to be responsible in some of the cases. According to Falta, the patients described by Léri, Gandy, Claude and Gougerot, and Cordier and Rebattu, belong in this group.

The cases hitherto described have nearly all been in males. The few cases described in females are not pure cases, but are instances of "multiple sclerosis of the endocrine glands" (Falta).

The diminution in the size of the testicles, scrotum and penis is often striking. Libido and potentia diminish. The cremaster reflexes are enfeebled. The skin of the face is pale and delicate. The hair of the head is dry. The secondary sexual hairs fall out. Masses of fat of peculiar distribution appear. The voice becomes higher pitched.

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## J. Infantilism

The term *infantilism* has been used in a very loose way. It originated with Lorain, who described one form, since known as **Lorain's type**, characterized by "debility, a gracile and small body, and a kind of arrest of development that affects rather the total mass of the person than any special apparatus"; in other words, in Lorain's infantilism, the person is affected by "a persistent juvenility that delays indefinitely in him the integral establishment of puberty." Since Lorain's paper, a whole series of conditions have been described as forms of infantilism (*e. g.*, infantilism with gigantism, or eunuchoid giants; late eunuchoids; multiglandular syndrome, etc.).

Fig. 685.—Case of Infantilism with Absence of the Thyroid and Tumor of the Pituitary. (After I. I. Lemann and R. M. Van Wart, Arch. Int. Med.)

Brissaud regarded Lorain's type as a dystrophic state, due either to a chronic congenital disease, or to some disease acquired during the growth period. Referring to examples of Lorain's type, he says they are "small, delicate persons, with thin, pale skin, long extremities, an infantile pelvis, a high-pitched voice, and a long neck; the epiphyses close at the normal time." His figurative sentence has been much quoted: "the fruit is ripe, but it is a small sample."

In contrast with the Lorain type, Brissaud described another type for which he thinks the term infantilism better suited.

In **Brissaud's myxinfantile type** the face is round, the lips thick, the nose small, the cheeks thick, the genitals infantile, the thyroid small, the ossification delayed, the second dentition delayed or absent, and the neck short; lumbar lordosis is common; there is a delay in the appearance of the ossification centers, and delayed epiphyseal closure. This condition Brissaud believes to be due to thyroid insufficiency, but his theory has been much disputed.

It is best, perhaps, at present to limit the term infantilism, with Falta,

to cases in which there is an arrest of development at some infantile stage, this arrest involving:

1. Faulty development of the genitals and of the vita sexualis, including the secondary sexual characters;
2. Faulty involution of the lymphatic apparatus;
3. Delayed growth and ossification;
4. Retention in whole, or in part, of the infantile dimensions of the body, the lower length remaining equal to the upper length or a little in excess of it, and the form of the pelvis remaining infantile, becoming neither male nor female in type; and
5. Retention of the infantile psyche.

The diagnosis of well-developed genuine infantilism should not be difficult, but confusion, with some of the states that closely resemble it, is easily possible in non-typical cases.

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## K. Multiglandular Syndromes

In the preceding sections, we have dealt with the clinical syndromes in which one of the endocrine glands has been primarily, or predominantly, diseased. There is a group of cases, however, in which *several endocrine glands seem to be simultaneously involved* in a sclerotic or an atrophic process. Obviously, very different clinical pictures may result, depending upon the varying insufficiency of the several glands. For such conditions the term *insuffisance pluriglandulaire* has been introduced by Claude and Gourgerot, whereas Falta applies to them the term *multiple Blutdrüsensklerose.*

As examples of the different pluriglandular syndromes that have been described may be mentioned the following: (1) acromegaly combined with symptoms of Graves' disease, (2) Graves' disease combined with outspoken symptoms of suprarenal insufficiency, (3) myxedema, or Addison's disease, combined with genital disturbances, and (4) syndromes suggesting simultaneous involvement of the thyroid gland, the gonads and the chromaffin system.

Such conditions are prone to occur in certain families, the predisposition being inherited and the symptoms coming out under the influence of some exciting cause such as alcoholism, various forms of intoxication, or acute infections, but, especially, in association with syphilis or tuberculosis. In other words, these multiglandular syndromes are pathological processes for the development of which a general constitutional inferiority is responsible, the actual exciting cause being some noxa that limits the function of the constitutionally feeble glands (Wiesel).

The association of multiglandular syndromes with cirrhosis of the liver has repeatedly been observed (Sourdel).

One of the commonest of the multiglandular syndromes, judging by the recent literature, is the so-called *thyrotesticularhypophyseal* (*suprarenal*) *syndrome.* It affects most often men between 25 and 30 who have, up to that time, developed apparently normally. Many of the patients are married men and the fathers of children. After some exciting cause, the patients begin to tire easily and to show aboulia, or the hair may fall out early. In other cases, loss of libido or of potentia is an early sign.

Many patients complain of indigestion, suffering from anorexia and vomiting without apparent cause, as in Addison's disease. These patients emaciate, and the skin assumes a sallow tint. Sometimes there is a general thickening of the skin.

In external appearance, most of these patients resemble the eunuchoids (absence of hair on the face, pallor, dryness, sallowness, abnormal wrinkling). The lower lip is often thick and prominent as in myxedema. The skin of the body may be translucent and devoid of pigment, in contrast with the yellowish or brownish pigmentation of the face. The external genitals are small. The pigmentation about the nipples may disappear. There is no struma, the thyroid being small and tough. There is often wasting of the muscles.

These patients are often classed among the neurasthenics. They tend to be apathetic and weak, especially during the morning hours. They complain of headaches and of feeling cold. They may suffer from hypochondriacal or persecutory ideas. Sometimes the psyche shows infantile traits (weeping spells, faulty inhibition, capricious moods). Polyuria, polydipsia or diarrhea may be prominent symptoms. Bradycardia and arterial hypotension are common. Vasomotor disturbances, like acroparesthesia, erythromelalgia and symptoms of Raynaud's disease are occasionally met with. The blood often shows a mononucleosis with eosinophilia. Trophic disturbances of the teeth and nails are not uncommon. The progress of the disease may be continuous or intermittent.

In the analysis of such multiglandular syndromes, it is customary to attribute the loss of the secondary sexual characters and of the sexual powers to changes in the *gonads;* the falling out of the hair of the scalp, the changes in the teeth, the dry skin, and the mental disturbances to the *thyroid gland.* Whether the myxedemalike condition of the skin is thyrogenic or hypophysogenic is not certain. The polyuria and the rapidly advancing cachexia are usually attributed to the *hypophysis,* while marked asthenia, hypotonia and abnormal pigmentations are ascribed to the anomaly of the *chromaffin system,* and the *interrenal system.*

A *second clinical type,* fairly well characterized, is the *thyrogenitochromaffin syndrome,* in which there are marked alterations in the pigmentation of the skin combined with symptoms of Graves' disease and certain eunuchoid traits.

A *third type* includes cases that suggest a combination of myxedema with hypophyseal insufficiency.

A *fourth type* includes cases presenting acromegalic changes combined with genital and gastro-intestinal disturbances, hypertrophy of the breasts, pigmentations, asthenia and often distinct signs of hypophyseal tumor.

These cases of multiglandular syndrome are separable from myxedema proper, since, in the latter, women are more often affected than men, the symptoms develop more quickly, and the mental changes are more marked, while the genital disturbances are less severe. Thyroid extract, very helpful in myxedema, does but little good in the multiglandular syndromes.

Typical Addison's disease and hypophyseal tumor can, usually, be easily ruled out.

In infantilism, the small body and delicate limbs are characteristic; in the multiglandular diseases, the general proportions of the normal body are maintained. The senile look of multiglandular diseases is not met with in true infantilism according to Falta, who thinks it unfortunate that the term *late* or *reversive infantilism* has sometimes been used to designate the multiglandular syndromes.

In cases that have come to autopsy, *sclerotic processes* have been found involving, almost equally, the thyroid gland, the ovaries or testicles, the hypophysis, and the adrenals. Chronic pancreatitis and hepatic cirrhosis have sometimes been associated. According to Wiesel, this change in the endocrine glands may be regarded as an end-stage of Bartel's status hypoplasticus. Wiesel prefers to designate the condition "a connective tissue diathesis of several endocrine glands," and hints that it may be the result of a disease of a single gland that has to do with the regulation of connective tissue growth, a kind of *senium precox.*

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